DOES NOT CIRCULATE

UNIVERSITY OF MICHIGAN
JAN 11 1955
MEDICAL LIBRARY

Journal of clinical and experimental Psychopathology & Quarterly Review of Psychiatry and Neurology

SYMPOSIUM ON PHYSIODYNAMIC THERAPIES IN PSYCHIATRY. PART I.

EDITORIAL: THE PHILOSOPHY OF ORGANICISM IN PSYCHIATRY
ELECTROSHOCK THERAPY — *Ugo Cerletti*
THE CONVULSIVE TREATMENT *and* THE CARBON DIOXIDE TREATMENT — *L. J. Meduna*
THE CLASSICAL SAKEL SHOCK TREATMENT — *Manfred Sakel*

VOLUME FIFTEEN, NUMBER THREE, JULY-SEPTEMBER, 1954

Statement of Purposes

The JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY and QUARTERLY REVIEW OF PSYCHIATRY and NEUROLOGY are dedicated to the search for the fundamental factors in the etiology and pathogenesis of psychiatric disorders; to the training of an alert, progressive, and qualified psychiatric personnel; and to the stimulation and support of all phases of psychiatric service and research—biologic, chemical, psychologic, physiologic, and social.

In the pursuit of these aims, the JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY and QUARTERLY REVIEW OF PSYCHIATRY and NEUROLOGY will venture wherever the quest may lead. Its sole criterion will be the promise of an increment in the understanding of the mind's ills. It will seek, above all, to bridge national boundaries, language barriers, and the artificial demarcations of schools and trends.

The JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY and QUARTERLY REVIEW OF PSYCHIATRY and NEUROLOGY hold that there is no justification for the present discrepancy between the rich scientific technology available to psychiatry and the poverty of technics in current use in diagnosis, treatment, and research; no need for the gap between the promise of research and the paralysis of inquiry; no excuse for the lag of years between discovery and publication, demonstration and application in practice; no sound reason for the tragic chasm between the desire of the public for psychiatric education and guidance and the failure of the profession to provide the inspiration and leadership that would fully mobilize all latent potentialities. In brief, the journal is dedicated to the fulfillment of psychiatry as a science and a humanity devoted to the interests of all mankind.

The JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY and QUARTERLY REVIEW OF PSYCHIATRY and NEUROLOGY look on psychiatry as an integral whole that is, in turn, an organic part of the world of science. It seeks to be not a mere sheaf of passive paper, but a dynamic organism by means of which its editorial board will endeavor to utilize every opportunity and facility in the field of human knowledge to fulfill the tasks to which it is dedicated.

JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY

&

QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

*

VOLUME XV, NUMBER 3, JULY–SEPTEMBER, 1954

JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY

ARTHUR M. SACKLER, M.D.—*Editor in Chief*
Director, Research Division, The Creedmoor Institute for Psychobiologic Studies

*

QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

WINFRED OVERHOLSER, M.D.—*Editor in Chief*
Professor of Psychiatry, George Washington University School of Medicine
Superintendent of St. Elizabeths Hospital, Washington, D. C.

Published Quarterly by

MD PUBLICATIONS, Inc.

Félix Martí-Ibáñez, M.D., *President*

Editorial and Advertising Offices
30 East 60th Street
New York 22, N. Y.

Circulation Offices
910 17th St., N.W.
Washington, D. C.

30 East 60th Street
New York 22, N. Y.

The Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology is published in March, June, September, December. A cumulative index is bound in the December issue. The subscription rates are $11.00 per year; $28.00 for three years. Entered as second class matter at the Post Office at Washington, D. C., under act of March 3, 1879. Published by MD Publications, Inc., 910 17th Street, N.W., Washington, D.C. Copyright 1954 by MD Publications, Inc. Printed in U. S. A.

JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY

ARTHUR M. SACKLER, M.D.—*Editor-in-Chief*
Director, Research Division, The Creedmoor Institute for Psychobiologic Studies

*

INTERNATIONAL EDITORIAL BOARD

DR. MANFRED BLEULER
University of Zurich, Zurich, Switzerland

DR. TÖRBJORN OSCAR CASPERSSON
Institute for Cell Research and Genetics
Karolinska Institutet
Stockholm, Sweden

DR. ROBERT A. CLEGHORN
1025 Pine Avenue W., Montreal, Quebec, Canada

DR. UGO CERLETTI
Clinica delle Malattie Nervose e Mentali
Viale dell Universita, 30
Rome, Italy

PROF. JEAN DELAY
Hôpital Psychiatrique, Paris, France

PROF. HONORIO DELGADO
Edificio, Belen 7, Lima, Peru

DR. HENRI EY
1 Rue Cabanis, Paris (14e), France

DR. M. FIAMBERTI
Vareze, Italy

DR. DIOGO FURTADO
Casal Ribeiro 12, Lisbon, Portugal

DR. FRITS GREWEL
Psychiatrische Kliniek (Pavill. III)
Wilhelmina-Gasthuis
Amsterdam W, The Netherlands

PROF. DR. L. VAN DER HORST
University of Amsterdam
Amsterdam W., The Netherlands

DR. B. JACOBOWSKY
Uppsala University, Uppsala, Sweden

DR. EMILIO MIRA Y LÓPEZ
Rua Candelaria 6
Rio de Janeiro, Brazil

DR. A. D. DE EGAS MONIZ
Santa Marta Hospital
Lisbon, Portugal

PROF. A. VALLEJO NÁGERA
Alcalá Galiano 8, Madrid, Spain

DR. MAX REISS
Research Department, Bristol Mental Hospitals
Fishponds, Bristol, England

PROF. FINN RUD
Universitetet I Bergen, Psykiatrisk Institutt
Neevengarden sykehus, Bergen, Norway

PROF. RAMON SARRO
Barcelona, Spain

International Editor
FÉLIX MARTÍ-IBÁÑEZ, M.D.
30 East 60th St.
New York 22, N. Y.

INTERNATIONAL RECORD OF CLINICAL AND RESEARCH PSYCHIATRY

NATIONAL EDITORIAL BOARD

PERCIVAL BAILEY, M.D.
912 S. Wood Street, Chicago, Illinois

JOSEPH BORKIN
1017 Ring Building, Washington 6, D. C.

FRANCIS J. BRACELAND, M.D.
Hartford Retreat, Hartford, Conn.

WALTER BROMBERG, M.D.
140 North Virginia Street, Reno, Nevada

HERVEY M. CLECKLEY
University Hospital, Augusta, Georgia

JACOB H. CONN, M.D.
Johns Hopkins Hospital, Baltimore, Maryland

GEORGE DEVEREUX, PH.D.
Devereux Foundation
Devon, Pennsylvania

RUDOLF DREIKURS, M.D.
25 East Washington Street, Chicago 2, Illinois

ERIKA FROMM, PH.D.
Institute for Juvenile Research, Chicago, Illinois

LEONARD GILMAN, M.D.
6 South Fullerton Avenue, Montclair, N. J.

LEO KANNER, M.D.
Johns Hopkins Hospital, Baltimore, Maryland

HARRY A. LA BURT, M.D.
Creedmoor State Hospital
Queens Village 8, L. I., New York

H. B. LANG, M.D.
Dept. of Mental Hygiene
State of New York, Albany, New York

WILLIAM MALAMUD, M.D.
Boston University School of Medicine
80 East Concord Street, Boston 18, Mass.

SYDNEY B. MAUGHS, M.D.
4500 West Pine Avenue, St. Louis, Missouri

L. J. MEDUNA, M.D.
Willoughby Tower
8 South Michigan Avenue, Chicago 3, Illinois

MERRILL MOORE, M.D.
382 Commonwealth Avenue, Boston 15, Mass.

MORTIMER D. SACKLER, M.D.
New York, N. Y.

RAYMOND R. SACKLER, M.D.
New York, N. Y.

MANFRED SAKEL, M.D.
550 Park Avenue, New York, New York

R. BURKE SUTTT, M.D.
Duke University School of Medicine
Durham, North Carolina

LAWRENCE F. WOOLLEY, M.D.
490 Peachtree Street, N.E., Atlanta, Georgia

S. BERNARD WORTIS, M.D.
410 East 57th Street, New York, New York

*

The *Journal of Clinical and Experimental Psychopathology* was founded in 1939 by V. C. Branham, M.D., as the *Journal of Criminal Psychopathology*. In 1944 the title was changed to the *Journal of Clinical Psychopathology*: in 1951 the journal became the *Journal of Clinical and Experimental Psychopathology*. The present title (*Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology*) was assumed in 1954.

JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY

*

The Philosophy of Organicism in Psychiatry 179
Félix Martí-Ibáñez, Raymond R. Sackler, Arthur M. Sackler, and Mortimer D. Sackler

SYMPOSIUM ON PHYSIODYNAMIC THERAPIES IN PSYCHIATRY

PART I.*

Electroshock Therapy 191
Ugo Cerletti

The Convulsive Treatment 219
L. J. Meduna

The Carbon Dioxide Treatment 235
L. J. Meduna

The Classical Sakel Shock Treatment 255
Manfred Sakel

Biographical Notes

Ugo Cerletti 317

Joseph L. Meduna 318

Manfred J. Sakel 319

* Part II of the Symposium on Physiodynamic Therapies in Psychiatry, which is to be published in the October-December issue of this journal, will contain the following papers: *Hormone Therapy* by Roy G. Hoskins; *How I Succeeded in Performing the Prefrontal Leukotomy* by Egas Moniz; *Prolonged Sleep Therapy* by J. Klaesi; *The Newest Physiodynamic Therapeutic Trends in Psychiatry* by Mortimer D. Sackler, Félix Martí-Ibáñez, Raymond R. Sackler, and Arthur M. Sackler.

QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

*

Incorporating the International Record of Psychiatry and Neurology

ARTICLE

Countertransference: Its Influence On A Patient's Capacity for Awareness 323
Daniel S. Jaffe

PSYCHIATRY ABSTRACTS

Administrative Psychiatry and Legal Aspects of Psychiatry

Medical Expert Testimony and Its Improvement 328
Psychiatry and the Law 328
A Study of Administration of Psychiatric Services 328

Biochemical, Endocrinologic, and Metabolic Aspects

The Significance of Amino-Acids in Neuro-Psychiatric Diseases 328
Effect of L (+) Glutamic Acid on Mental Growth 329
A Review: Psychological Responses to ACTH, Cortisone and Related Steroid Substances 329
Schizophrenia: A New Approach. II. Result of a Year's Research 330
Three-Year Follow-Up of Patients Developing Eosinophilia During Insulin Coma Therapy 331
On Pathologic Metabolic Conditions in Cases of Compulsive Neuroses 332

Clinical Psychiatry

The Recognition and Treatment of Anxiety States 332
Major Neuropsychiatric Residuals Following Resuscitation from Cardiac Arrest; Preliminary Observations with Report of Three Cases 335
Psychiatric Observations in Neurocirculatory Asthenia 335
The Initial Interview 336
The Concept of Emotional Allergy 336
On the Problem of Schizophrenia from the Point of View of Welfare Medicine 337
Delusion of Parasitosis; Report of Successful Care with Antipellagrous Treatment 337
Effect of Amobarital (AMYTAL) and Affect on Conceptual Thinking in Schizophrenia, Depression, and Neurosis 338

Heredity, Eugenics, and Constitution

The Cerebral Ventricles in Dementia Praecox 338

Psychiatry and General Medicine

The Treatment of Psychosomatic Disorders by the Internist 339
Somatopsychic Medicine 339
Psychologic Implications of Cancer 340
The Importance of Depressive Reactions in Clinical Medicine 340

Psychologic Methods

Results of the Rorschach Test Given to Obsessional Neurotics 340
The Varying Response to Pain in Psychiatric Disorders: A Study in Abnormal Psychology 340

Psychopathology

A Re-examination of Some Aspects of Conversion Hysteria ... 342
Psychotherapy of Schizophrenia and Borderline Cases ... 342
On Creative Functions in the Beginning of Schizophrenic Psychoses ... 343
The Transition of Obsession Neuroses into Schizophrenia in the Light of the Catamnesis ... 344
On the "Anatomy" of Hypochondriac Conditions ... 344
The Application of Cybernetics to Psychiatry ... 345
Depression, Hypomania and Depersonalization ... 345

Treatment

A. General Psychiatric Therapy

The Conditioned Reflex in the Chronic Schizophrenic ... 346
Treatment of Elderly Psychiatric Patients; Use of a Diagnostic Classification ... 347

B. Drug Therapies

Chlorpromazine; New Inhibiting Agent for Psychomotor Excitement and Manic States ... 347
The Effect of Drugs on Group Therapy: An Experiment ... 349

NEUROLOGY ABSTRACTS

Clinical Neurology

Clinical Observations on Aphasia ... 350
Observations on the Different Diagnoses of Multiple Sclerosis and Pernicious Anemia, with Special Consideration of the Early Stages ... 350
Pyramidal Signs ... 351
Spontaneous Rhythmic Ocular Movements; Their Possible Relationship to Mental Activity ... 352

Anatomy and Physiology of the Nervous System

Recent Advances in Neurophysiology ... 352
Further Analysis of the Temporal Lobe Syndrome Utilizing Frontotemporal Ablations ... 353

Convulsive Disorders

Incidence of Idiopathic Convulsions in Later Life ... 353

Degenerative Diseases of the Nervous System

Is Multiple Sclerosis a Manifestation of Idioblaptic Allergy? ... 354
Liver Function and Other Blood Chemistry Tests in Multiple Sclerosis ... 354

Electroencephalography

The Electroencephalogram in Pernicious Anemia and Subacute Combined Degeneration of the Cord ... 355
The Electroencephalogram in Paralysis Agitans ... 356
The Electroencephalogram in Manic-Depressive Psychosis ... 356
Clinical Evaluation of Metrazol Activation in Electroencephalography ... 357

Treatment

On the Medicinal Treatment of Myasthenia ... 358
Experiences with RO-2-3059 as an Anticonvulsant ... 359

BOOK REVIEWS

Man Above Humanity: A History of Psychotherapy ... 359
The Sexual Offender and His Offenses ... 360
Fifty Years of Medicine ... 360
The Psychiatric Aide: His Part in Patient Care ... 361
Syphilitic Optic Atrophy ... 361
Fundamentals of Neuropathology ... 362
Books Received for Review ... 362

Instructions to Contributors

All manuscripts submitted for publication in JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY AND QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY should be sent to Dr. Félix Martí-Ibáñez, 30 East 60th Street, New York, N. Y. Manuscripts should not include data published previously and it is understood that any manuscript submitted is not being submitted elsewhere.

Manuscripts.—All manuscripts should be typewritten, double-spaced, on only one side of paper 8½ by 11 inches in size. They should be mailed in a flat package. *The original and two copies are required.* Original drawings or tracings should not be sent. Glossy photographs, no larger than the manuscript paper, of all illustrations should accompany the copies of the manuscript. Prints should be sufficiently clear to permit the making of engraver's cuts without retouching and to allow reduction to approximately ½ size.

Tables, figures, charts, etc., must be typewritten on separate sheets and should be placed in proper sequence in the manuscript. Numerals are used for figures for all definite weights, measurements, percentages, and degrees of temperature. All indefinite and approximate periods of time and other numerals which are used in a general manner should be spelled out. Standard abbreviations should be used whenever weights and measurements are given in the metric system. The forms to be used are: Gm., ml., Kg., mg., mcg., mm., and l. Per cent should be written out in the text.

Footnotes and Bibliographies should conform to the style of the Quarterly Cumulative Index Medicus published by the American Medical Association. This requires, in the order given, last name of author, initials, title of article in the language in which it was written, name of journal with accepted abbreviation, volume number, and year. Footnotes should not be included in the text pages. All references are to be numbered consecutively and typed on a separate sheet.

Summary.—Each manuscript should conclude with a brief summary, appropriate to the length of the article, but in no case to exceed 300 words.

Illustrations.—A reasonable number of half-tone illustrations will be reproduced free of cost to the author but special arrangements must be made with the editor for color plates, elaborate tables, or extra illustrations. Pen drawings and charts should be drawn and lettered only in India ink or black typewriter ribbon (when the typewriter is used). Only good photographic prints or drawings should be supplied for half-tone work. All photographs submitted should be numbered and bear on the back author's name, address and title of article. Top of the picture should be indicated.

Reprints.—Authors will be sent an estimate of the cost of reprints with galley proofs. Reprints may be ordered at any time after manuscript has been set in type but not later than 30 days after the JOURNAL has been published.

Contributions in a Foreign Language, if found suitable for the JOURNAL, will be translated at the expense of the JOURNAL.

Business Communications.—All communications in regard to advertising, subscription, change of address, etc., should be addressed to MD Publications, Inc., 30 East 60th Street, New York 22, N. Y. The publisher should be advised of a change in the subscriber's address about 15 days before the date of issue of the JOURNAL with both new and old addresses given.

Subscription Rates.—In the United States, $11.00 per year, $28 for three years. Remittance for subscriptions should be made by check, draft, post office or express money order payable to MD Publications, Inc.

Announcing Publication of the Book

SYMPOSIUM ON PHYSIODYNAMIC THERAPIES IN PSYCHIATRY

This historical Symposium on Physiodynamic Therapies in Psychiatry will be published *as a clothbound book* which will contain all the papers in both Part I and Part II of the Symposium. It will be one of the most valued reference works in the library of the psychiatrist, the physician, the researcher and the clinician. This is the first time that the great discoverers of the somatotherapies have presented their works together in one volume. The *Symposium On Physiodynamic Therapies* will contain the following articles:

Electroshock Therapy by Ugo Cerletti

Hormone Therapy by Roy G. Hoskins

Prolonged Sleep Therapy by J. Klaesi

The Convulsive Treatment and The Carbon Dioxide Treatment by L. J. Meduna

How I Succeeded in Performing the Prefrontal Leukotomy by Egas Moniz

The Classical Sakel Shock Treatment by Manfred Sakel

The Philosophy of Organicism in Psychiatry by Félix Martí-Ibáñez, Raymond R. Sackler, Arthur M. Sackler, and Mortimer D. Sackler

The Newest Physiodynamic Therapeutic Trends in Psychiatry by Mortimer D. Sackler, Félix Martí-Ibáñez, Raymond R. Sackler, and Arthur M. Sackler

For more information on the publication date and cost of the clothbound edition of the *Symposium on Physiodynamic Therapies in Psychiatry*, please fill in the coupon below and return it to MD Publications, Inc., 30 East 60th Street, New York 22, New York. Since this book will be published in only a limited number of copies, please mail the coupon requesting further information at once.

Please send me complete information on the clothbound edition of *Symposium on Physiodynamic Therapies in Psychiatry.*

Name .....

Street .....

City ..... Zone ..... State .....

Mail this coupon to MD Publications, Inc., 30 East 60th Street, New York 22, N. Y.

JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY
&
QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

*

The Philosophy of Organicism in Psychiatry

Félix Martí-Ibáñez, M.D., Raymond R. Sackler, M.D., Arthur M. Sackler, M.D., and Mortimer D. Sackler, M.D.

THE VAN OPHUIJSEN CENTER
NEW YORK, N. Y.

I. THE CONCEPT OF THE MIND IN CLASSICAL GREECE

Discipulus est priori posterior dies—each day is the scholar of yesterday. To understand better the transcendental importance in modern medicine of the new psychiatric somatotherapies, one must study the evolution of the philosophical thought that led from the mystic shadows, which for so many millennia obscured the concept of mental illness, to the radiant dawn of modern psychiatric therapy. Although the application of these therapeutic methods dates back less than a quarter of a century, philosophically they represent the crystallization of a thought with a history of more than twenty-six centuries.

Let us, therefore, first of all, outline the evolution of the organicistic concept of the human mind: the historical trajectory of the idea—which today seems elementary, yet for so many centuries was considered revolutionary—that the brain is the core of the mind. Following this, we shall trace the historical roots of the forms of therapy based on the somatic treatment of mental diseases. Historically and philosophically, one concept presupposes

the other. For once the brain was recognized as the core of the mind, it became logical to treat mental disturbances by therapies intended to correct alterations in the cerebral tissues.

Some five hundred years before Christ, the figure of Alcmaeon of Crotona, pupil of Pythagoras, emerged on the horizon of history. His work entitled *Concerning Nature* was the basic text book on medicine prior to Hippocrates. Alcmaeon of Crotona declared that the brain, not the heart, was the organ of the mind, and that through it, sensorial impressions reached our consciousness. A physiologist of stature, he carried out experimental studies on the functional alterations caused by brain lesions. But his viewpoint, an isolated beacon in an age clouded by the fog of mysticism, was not shared by his contemporaries or by the majority of Greek philosophers who followed him. Their favorite pastime was to discuss endlessly the nature and core of the consciousness and the mind, ascribing intelligence, passions, and sensibility to such organs as the heart, liver, and lungs.

The true founder of anatomiconeurological thought in psychiatry, however, was Hippocrates (c. 460 B.C.–355 B.C.), who held the view that psychic functions had a cerebral substratum, a concept accepted by Aristotle (384–322 B.C.) and Herophilus and Erasistratus (c. 310–250 B.C.). Hippocratic thought, which was naturalistic in outlook, was based on observation and experimentation at the patient's bedside.[1] It challenged the mysticism of the Asclepiades by insisting that mental disturbances resided in the brain, thus opposing the prevailing belief in demonism with its natural-physical doctrine of psychopathological alteration.

In *The Sacred Disease*, Hippocrates states: "Men ought to know that from the brain and from the brain only arise our pleasures, joys, laughter, and jests as well as our sorrows, pains, griefs and tears. . . . It is the same thing which makes us mad or delirious, inspires us with dread and fear, whether by night or by day, brings sleeplessness, inopportune mistakes, aimless anxieties, absent mindedness and acts that are contrary to habit . . . . Madness comes from moistness. When the brain is abnormally moist, of necessity it moves, and when it moves neither sight nor hearing are still but we see or hear now one thing and now another, and the tongue speaks in accordance with what has been seen and heard on any occasion . . . ."

Hippocrates declared that intelligence reached the brain borne by the air that circulated through the veins—for such was the accepted explanation of circulation at that time—and that when the veins were obstructed by cold phlegm, the patient lost consciousness, and an epileptic seizure ensued. In attributing the latter to irritation of the brain by acid or sour substances, Hippocrates established the first indication recorded in history of the localization in the brain of certain pathological processes of the mind. He also described mania, "phrenitis" melancholia, puerperal psychosis, and hysterical phenomena. To treat mental diseases he used physical and chemical medications, such as rest, baths, a bland diet, purgatives and emetics, and extracts of plants, such as black hellebore and mandrake, for their cardiotonic, narcotic and gastrointestinal effects.

The doctrines of Hippocrates and the earlier ideas of Alcmaeon of Crotona subsequently influenced Plato (427–347 B.C.), the portentous Athenian who emblazoned the Golden Age of Pericles. Plato also believed that the core of intelligence—and of its disturbed form,

insanity—was the brain. He attributed epilepsy to the obstruction of circulation of air in the head by a mixture of white phlegm and black bile. Commenting on Aristole's concept that the sole function of the brain was to cool and purify the air or vapors carried by the blood through the veins to the brain, Plato, in his *Phaedo*, has Socrates say: "It is the brain which creates the sensations of hearing, sight and smell, from which arise, in turn, memory and reasoning; and from these sensations, once they are established, knowledge is born. . . . There is no cure for the body apart from the mind. First, then, and above all, the mind must be treated if the body is ever to be made whole. . . . Just here the mistake is made in regard to man: the attempt to treat the body independently of the mind." In these words Plato condensed the Greek credo that all the illnesses of man were psychosomatic in nature, a thesis which is accepted today by a number of schools of psychiatry.

Asclepiades of Bithynia (c. 124 B.C.) classified insanity into acute and chronic; while Aretaeus of Cappadocia (c. early second century A.D.) recorded clinical descriptions of cerebral palsy and in his lifetime spread the views of Hippocrates concerning the brain. The elegant Celsus (first century A.D.), the Cicero of medicine and possibly the greatest medical mind in classical Italy, studied hallucinations and deliriums and described the neurovegetative functions in the insane.

II. FROM GALEN TO STENSEN

This gigantic wave of naturalistic doctrines concerning the brain, the mind, and mental disturbances, was confirmed and supported by Galen (138–201 A.D.), who maintained that the brain was the organ of the mind and of all sensation and movement. This concept of the Roman Dictator of Medicine persisted through the centuries that followed[2] despite the fact that during this era (with the exception of the concept of cerebral localizations worked out by Constantine the African (1015–1087) and a few sporadic references by Arab authors[3] to the cerebral localization of mental disturbances) organicist thought in psychiatry lapsed into the lethargy of the long medieval night, lulled into slumber by the chants of religious fanaticism and demonism.[4]

Since the Church regarded suspiciously any opinions that did not agree with its notions of witchcraft and demons as the only explanation for mental diseases, physicians had to fumble along as best they could. For many centuries, observation and experiment were replaced by the dogmatic authority of the classic writers. As Sir Thomas Browne was later to say in his *Religio Medici*, authority has ever been "a powerful enemy unto knowledge."

In his *De Humani Corporis Fabrica*, prelude to modern science, Vesalius (1514–1564) reaffirmed the possibility of the cerebral localization of mental diseases. A contemporary of Vesalius, Johann Weyer, is considered by some authors as the father of modern psychiatry. In his book entitled *De proestigis doemonum*, Weyer assailed the welter of belief in devils and witchcraft which prevailed in his day. Along with his precise clinical descriptions of mental patients, he launched a crusade against the Inquisition and its methods of torturing the insane as creatures possessed of the devil, thereby introducing humanitarianism in the care of the mentally sick.[5]

At a time when the Renaissance[6] was radiating its beams of clarity to the farthest reaches of Europe, the French philosopher René Descartes (1596–1650) dedicated his years of voluntary exile in Amsterdam and Sweden (from 1628 until his death) to solving by mathematical methods the problems of biology and medicine, supported by anatomical observations. To this very day, medicine is influenced by his philosophical system, which is known as Cartesianism and directly linked with the ideas of Giordano Bruno (1548–1600). Descartes liked to wander along the sleepy, melancholy streets of old Amsterdam, collecting anatomical specimens from butcher shops, which he would take to his room to dissect. In a treatise on physiology, *De Homine*, forerunner of the philosophies of iatrochemistry and iatrophysics, he localized the soul in the pineal body.

At about this same time, Niels Steno (Stensen) (1638–1686), discoverer of the parotid and lacrimal ducts, in a discourse delivered in 1665 in Paris at the home of Melchisédech Thévenot, patron of the sciences, declared: ". . . Those who seek for solid knowledge will find nothing to satisfy in all that has been written about the Brain, but it is, quite certainly, the principal organ of the soul and the Instrument which works very wonderful effects."

This prevailing ideology subsequently had a brilliant supporter in Georg Stahl (1660–1734), founder of animism and one of the precursors of biological medicine. Stahl distinguished between delirium due to physical causes and that due to emotional causes. He fought to achieve recognition of the integral unity of man as against the concept of dualism between mind and body, which in his day reigned supreme.

III. FROM MORGAGNI TO PINEL

Towering astride two centuries, the figure of Giovanni Battista Morgagni (1682–1771), who laid the anatomicopathological basis of modern medicine, stands forth as a revolutionary in the field of medical concepts. In his magnum opus entitled *De sedibus et causis morborum per anatomen indagatis* (1761), a monument of clinicopathological descriptions, he enunciated the concept of insanity as an organic disease. He introduced in medicine what Virchow later called "the anatomical concept in the study of disease."

Morgagni's views on anatomy were carried on by the French alienist Joseph Daquin (1733–1815). In his *Philosophie de la folie* (1791), Daquin recommended humanitarian treatment of the insane. He also warned against the excesses of anatomical interpretation of mental illnesses which were already beginning to be observed, stating: "A good many of the lesions found in the brains of the insane were, to all appearances and in all probability, not formed until the latter years of (the patient's) life and represent the effects rather than the cause of the disease."

Other authors who supported the anatomical concept of mental disturbances were Sementini (1743–1814) and the humanitarian Vincenzo Chiarugi (1759–1820). The latter wrote *Della pazzia in genere e in ispecie*, which is devoted to the diagnosis, prognosis, and pathological anatomy of mental diseases. They were followed by F. J. Gall (1758–1828), whose views on anatomy were to be confirmed a century later by Nissl and Ramón y Cajal.

Although he offered no proof of his statements, C. W. M. Jacobi (1775–1858) was the first German psychiatrist that presented systematically in his writings mental disturbances as

symptoms of disturbances in the functions of the brain, indicating that mental disease was a misnomer for what should be called brain disease.

The standard-bearer of vitalism, the anatomist J. C. Reil (1759–1813), described the structures of the cerebellum and the insula ("island of Reil"). He recorded a study of a process similar to the present-day concept of a psychoneurosis. During this same period, J. Haslam (1764–1826) described the syphilitic nature of dementia paralytica. Meanwhile, Phillipe Pinel (1745–1826), glorious liberator of the mental patient and initiator of a new era in humanitarian assistance, declared, in his *Traité médico-philosophique sur l'aliénation mentale* (1801), that mental diseases were based on pathological alterations of the brain.

IV. THE XIXTH CENTURY

In the nineteenth century, psychiatry acquired the category of an autonomous medical discipline. "From Hippocrates to Boerhaave," wrote Heinroth in 1818, "bile was the sole cause, melancholy and mania the sole effect, and the elimination of the peccant materia the sole remedy in mental disease."

Three German clinicians—Griesinger, Meynert, and Wernicke—started the parade of great scientific figures in the nineteenth century,—a century destined to see psychiatry established on firmer organic foundations. They studied and reported the anatomicopathological alterations that take place in the brain of mentally sick patients.

Wilhelm Griesinger (1817–1868), author of the first textbook on psychiatry (1845), sought to demonstrate that every psychosis is determined by specific cerebral lesions. Thus, he identified the activity of the psychiatrist with that of the physician treating diseases of the body and advocated common methods of investigation in the natural sciences.*

Theodor Meynert (1833–1892), a pupil of the great pathologist Rokitansky, studied the structures of the brain and the physiopathology of the nervous system in man and animals. He established the functional antagonism existing between the cerebral cortex and the deep cerebral nuclei, and emphasized the importance of cerebral circulatory disturbances in the genesis of mental disturbances. He is regarded by some authorities as the forerunner of modern investigators of cerebral cytoarchitecture and also of those who treat mental ailments with agents that modify the circulation and nutrition of the cerebral tissues.

Karl Wernicke (1848–1905) presented "focalist" concepts, many of which he supported with anatomicopathological evidence, and also published an excellent atlas of the brain.

Around the middle of the nineteenth century, German and French contributions reinforcing the organic concept of psychiatry began to spring up in greater number. Even as its influence was ebbing, the Romantic school of psychiatry in Germany was recreating the medicine of Paracelsus in the works of Neinroth and Gross. Some psychiatrists, such as Morel and Magnan, became partisan to the criteria of genetics and attributed mental disease to heredity in the sense of a degeneration or a polyvalent hereditary disposition, while others, like Krafft-Ebing, saw it as a pure encephalic lesion.

---

*Griesinger's pupil, Karl Westphal (1833–1890), specialized in the study of histopathological psychiatry.

The French psychiatry of the first half of the nineteenth century, as represented by Pinel, Esquirol (1722–1840), Georget and Fodéré, is rather equivalent in its nosology to the anatomical chapters into which works on pathology were divided prior to Sydenham.

In the latter part of the century, Liébeault (1825–1893), Charcot (1825–1893), and Bernheim (1840–1919) established the scientific bases of the use of hypnosis in psychiatry and medicine, giving stimulus to a psychological orientation in psychiatry. Paradoxically, we find the great neurologists, such as Charcot and Janet (1859–1947), encouraging the development of a psychological psychiatry! It was in this atmosphere of neuropsychiatrists obsessed by the desire to discover what the *species morbosae* of psychiatry was that the future psychogenic concepts of mental disease first began to germinate.

The historical delimitation of separate clinical entities within psychiatry was firmly underway at the turn of the century. This was necessary for the individualization of psychiatric therapy and for the establishment of therapy on a rational basis of the etiology and pathogenesis of each mental disease. Thus, the separation of dementia paralytica patients from the great mass of hospitalized psychotics was arrived at. Falret and others laid the foundations of clinical diagnostic criteria. It remained for Richard von Krafft-Ebing (1840–1902) to demonstrate the correlation existing between a syphilitic infection previously existent in a patient and subsequent dementia paralytica as established by the patient's immunological response to inoculation with *Treponema*. Subsequently, Aloys Alzheimer (1864–1915) described the histopathological alterations in cerebral syphilis, while Emil Kraepelin (1856–1926) established that a previous syphilitic infection is an indispensable condition for the development of dementia paralytica. Treponema was discovered in the brain of paretic patients by Noguchi and Moore. In 1910 Paul Ehrlich introduced salvarsan (arsphenamine) in the treatment of syphilis. Ehrlich's "magic bullet" was followed by malariotherapy, introduced in 1917 by J. von Wagner van Jauregg.*

Towards the end of the nineteenth century began the era of almost explosive progress in somatological psychiatry, starting with the monumental work of Emil Kraepelin. After elucidating the historically common elements in groups of psychotic patients, Kraepelin proposed a scientific nosology of the two main psychoses. As early as 1896, he began to develop the organophysiological concentration in psychiatry, systematizing it as a science. He gave it a pseudoclassical perfection in setting up, together with Kahlbaum, the "descriptive types" which are still basic in our present-day psychiatric classifications. In the later editions of his splendid textbook, Kraepelin, by integrating the somatological and psychological emphases, foreshadowed a metabolic trend, and thereby laid a biological basis for psychiatry.

As a corollary to this avalanche of somatological contributions to psychiatry stands the statement made by Professor Benedict before the International Congress of Psychiatry

---

* In this way, following delineation of etiological and pathogenetic mechanisms, a considerable part of the mentally ill population was afforded relief, later arrest of pathology, and in more recent days specific therapy and control. Of greater importance, late cerebral manifestations have been practically eliminated by proper prophylaxis and therapy with antibiotics.

held in Paris in 1899. After the great Korsakow (1854–1900) had finished reading his historical paper on "A Form of Mental Disease Combined with Degenerative Neuritis," Professor Benedict rose to remark: "We thank Dr. Korsakow for his interesting study. He has confirmed to the maximum the theory that all psychopathology can be reduced to lesions of the brain and the nervous tissues."

In 1890 Sigmund Freud (1856–1939) began his monumental contributions to the study of psychiatry. With Freud, psychologic psychiatry gained preeminence and a number of revolutionary contributions were introduced in medicine as they evolved in the development of psychoanalysis. Among these are:

(1) The description and definition of the unconscious and the important role of such psychic material in motivation of behavior; the formulation of the existence of various levels of psychological consciousness, namely, unconscious, preconscious and conscious;

(2) the concept of a "structural" stratification of the psyche with id, ego and superego;

(3) the psychosexual development through oral, anal and phallic stages in the achievement of adult genital sexuality as well as the concept of regression to earlier stages;

(4) the use of dialogue and free association—an outgrowth from his work with hypnosis in hysteria—as a therapeutic tool; the relationship of resistance and dreams to this procedure; the role of transference in the psychoanalytic process and its use by the therapist.

(5) the controversial concept of instinctual forces, including the libido, and their psychodynamic significance and therapeutic applicability.

Before Freud, hysteria, in the Charcot manner, was *ex visu;* since Freud, it has developed greater depth: *hysteria ex audita*. Pathology, before Freud, was observed as exclusively visual and tactile. Since Freud, the study of psychopathology gained an *auditive* dimension (symptom complexes are defined *ex audita*). Attention was directed to the zones of being and human life susceptible to verbal audition, comprehension and interpretation, but not to eidetic intuition. Freud's later years were marked by an orientation—also adopted later by Eugen Bleuler (1857–1939)—toward the integration of the somatological aspects within psychiatry and an ever more biological emphasis on psychological phenomena.

V. THE XXTH CENTURY: FOUR GIANTS

In the history of organicist ideas, psychiatry finds itself, in the twentieth century, beneath the brilliant constellation formed by the work of Freud; the transcendental achievements of Santiago Ramón y Cajal (1852–1934) in the histopathology of the nervous system, which were later to constitute a source of inspiration for the whole newer somatological approach to psychiatry; the work of J. P. Pavlov (1849–1936) on the physiology and physiopathology of the nervous system, with his studies of higher nervous functions through the use of his method of conditional reflexes; and the accomplishments of Charles S. Sherrington (1861–1952) demonstrating the complex integration of the nervous centers and their functions. The mere enumeration of these names is sufficient to constitute one of the most electrifying pages in the history of scientific progress. The genius of these investigators had as its common denominator the acceptance—even by Freud—of the premise that the substratum of

nervous diseases not due to structural alteration is a functional disturbance of the nervous tissues invisible to the microscope, but which may be revealed through biochemical analysis.

VI. THE PHILOSOPHICAL BASIS OF PHYSIODYNAMIC THERAPY

This concept of mental diseases having a physiopathological, organic, sometimes histological and always endocrinological and biochemical substratum served as a philosophical basis for the development of somatotherapies in psychiatry. In these newer treatments we cannot help but see the immense impact of the latest discoveries in histology, physiopathology, biochemistry, and physics upon psychiatric thinking.

The therapies embrace the modes of treatment that concentrate on the somatic substratum of the phenomenon of consciousness. Though the methods are empirical, they may help uncover physiopathological data and lead to greater specificity in the treatment of mental disease by physical means as well as biochemotherapeutically. These methods, which today are fundamental, particularly in the treatment of the more malignant disturbances, can be classified into three major groups, viz., physicotherapeutic, biochemotherapeutic and psychosurgical.

The treatment of insanity by means of agents which profoundly agitate the organism has been used in an infinite variety of empirical forms in all ages. Hippocrates, Galen and Boerhaave, in fact, mentioned cases of mental illnesses cured as a result of febrile diseases contracted at the same time as the mental process.

We cannot consider the trepanations so profusely recorded in prehistory—like the Peruvian *huacos*—as a forerunner of present-day somatotherapy, unless indirectly. For in primitive times disease was not regarded as a natural phenomenon, but as a religious and magical punishment. Trepanation was practiced to relieve those "possessed"—tormented by terrible headaches or by epilepsy—by opening a hole in their skull with a trepan or punch made of bone or sharp stone in order to allow the evil spirits possessing the subject to escape *from his head*, not from his brain, inasmuch as the latter organ was not recognized as the core of consciousness but only of the soul and of the spirits that possessed the soul.

Somatotherapies in psychiatry did not really begin until it was understood that just as disease cannot exist without a patient to suffer from it, so the mind—or mental disease—cannot exist without a brain. The human mind, in relation to a somatic structure, and its ailments affect the human being in his totality, the whole person, and not just his psyche. It is precisely because the psyche and the soma are simultaneously affected, however, that it was thought that even as physical disturbances could be corrected by treatment of the psyche, so probably could mental disturbances be corrected by the application of certain therapies to the brain and the body in general.

VII. THE HISTORICAL ANTECEDENTS OF SOMATOTHERAPY

The most ancient report in existence of the use of electroshock *before* the discovery of electricity was recounted by none other than the discoverer of present-day electroshock, Ugo Cerletti (b. 1877, in Italy). At the First International Congress of Psychiatry in Paris (1950), Cerletti reported that Scribonius Largus, physician to the Roman Emperor Claudius,

had written in his *Compositiones medicamentorum* the following: "A chronic and intolerable headache which insistently manifests itself can be eliminated at once if treated by applying a live torpedo fish (electric eel), black in color, to the site of the pain and leaving it there until the pain stops and the part is swollen (*obstupescat*). As soon as this occurs, the remedy should be removed, in order not to abolish sensibility in the region affected. It is necessary to prepare a certain number of these torpedo fish; for the benefit of the cure, or reactivation —which is the index of the utility of the effect obtained—is often only achieved after two or three applications."

The therapeutic nihilism which prevailed in psychiatry until well into the eighteenth century was interrupted only occasionally by some spark of light that anticipated the somatotherapies of the future. In 1804 Joseph Mason Cox, the English physician, in his booklet entitled *Practical Observations on Insanity*, stated: "It is evident that any considerable excitement, some new and violent action provoked in the course of the manic disease, often has the effect of considerably alleviating the mental disorder or of permanently improving it." Cox recommended the inoculation of smallpox or scabies, and irritation of the skin with emetic tartar, vesicants, or setons to produce suppuration.

Spasmo spasmus solvitur. . . . This same principle was reflected in the discovery—though not in the development—by G. Burrows, of London, of convulsive shock therapy in 1828, more than a century before its rediscovery in our times. In his *Commentaries on the Causes, Forms, Symptoms and Treatment, Moral or Medical, of Insanity*, he notes: "In a case of insanity in which two scruples (of camphorated oil) were applied, a convulsive seizure was produced, and a complete cure followed."

As early as 1845, Griesinger employed ether, chloroform, and opium in the treatment of psychotics. In 1870, Britsch and Hitzig, followed by Batelli, Viale, Chiauzzi, and others, studied the electrical stimulation of the cerebral cortex and the production of convulsive crises in man. In 1918, A. S. Loeveenhart made a study of the use of carbon dioxide in stimulating cerebral circulation in mental patients—twenty years before the rediscovery of the same treatment! Leduc, in 1902, succeeded in producing the inhibition of the cerebral hemispheres in mental patients, causing sleep and general anesthesia during the application of electric current to the cranium of his patients. Zimmerman and Dinier, in 1903, applied Leduc's method to produce epileptic coma experimentally by electricity years before the definitive contribution of electroshock therapy by Cerletti.

In its turn, the discovery by Klaesi (b. 1877, in Switzerland) in 1920 of *Dauernarkose*, or therapy by prolonged sleep, with the use of somnifene and dial, was preceded by the use of trional by Wolf in 1901 for the same purpose.

Insulin coma therapy, discovered by Sakel (b. 1900, in Austria), was historically preceded by G. Klemperer's (1865–1946) discovery that insulin improved the general state of mental patients by producing hypoglycemia, as well as by the doctrines of Pascal and Davesne concerning colloidoclastic shock.

Convulsive shock therapy with cardiazol, discovered by Meduna (b. 1896, in Hungary), had as a precedent, besides the curious experiments of Auembrugger—mentioned by Meduna himself—the observations in 1929 by Nyro and Jablonski concerning the effectiveness of

antiepileptic medication when epilepsy is associated with schizophrenia. G. Mueller reported (1930) 2 cases of catatonic schizophrenia which were cured upon development of epileptic convulsive crises. Glaidus (1931) cited 8 cases of epilepsy associated with schizophrenia in which there was an eruption of the schizophrenic symptoms when the epileptic ones disappeared. Comparable historical precedents could be listed in connection with the use of hormones in psychiatry.

The fact that a tree has deep roots does not detract from the importance of its fruits but, if anything, enhances it. To Cerletti, Klaesi, Meduna, Egas Moniz (b. 1874, in Portugal), and Sakel must go the glory of having introduced in modern psychiatry a series of somatotherapies which today make it possible to treat with greater success the two most important endogenous psychoses, schizophrenia and manic-depressive psychosis, as well as other neuroses.

Those somatotherapies also permit the introduction or continuance of psychotherapy by reintegrating and achieving reality in a psychotic patient when such therapy is excluded by the interference of a psychotic episode.

In 1934, Manfred Sakel, of Vienna, published his method of treating psychoses by producing a state of coma by means of insulin injections. The same year, Ladislaus von Meduna, of Budapest, reported his method of producing convulsive attacks through the injection of cardiazol. In 1935 Egas Moniz, of Lisbon, described his performance of the leukotomy (prefrontal lobotomy), thereby introducing surgery into the psychiatric field and creating the new specialization of psychosurgery. And in 1938, Ugo Cerletti and L. Bini, of Rome, demonstrated their electroshock technique.

Without going into the always delicate matter of historical priorities, the account of how these discoveries were arrived at and their reevaluation in the light of the score of years that have since elapsed is of great historical and practical importance. We are privileged to present such an appraisal in the following pages by the discoverers themselves.

To the achievements described should be added those that have been realized in the field of biochemical and endocrine therapy by Hoskins and several current groups of investigators, who are reviving the naturalist tradition in psychiatry by setting out to conquer mental diseases with organic methods. These investigators are using clinical and physiological data as their point of departure, with a view to discovering and developing new physiological and pharmacological agents.

Accomplishments in the field of somatotherapy in psychiatry may be likened to a majestic bridge having as its first pillar the historical therapies described; as its central pillar, the convulsive shock therapies and psychosurgery; and as its pillars still in the process of construction, the biochemical therapies (thyroid, testosterone, adrenal hormones, histamine, and acetylcholine) and, most recent of all, we hope, pharmacological therapies (chlorpromazine and Rauwolfia serpentina). It is not yet possible to see the completed bridge which will carry us to the shore of the future. But following with a visionary eye the sweeping curve of the unfinished bridge, it is possible to project it toward the future and to see that some day the remaining pillars will be completed. It will then be possible for Psychiatry to cross by the bridge of somatotherapy over the conquered waters of the restless river of mental disease.

NOTES

1. Hippocrates localized the residence of the soul in the brain: *"Cerebrum illuo organum est, ex quo insania originem ducit . . . Insanit homo ob humiditatem cerebri, in quo animi sunt officia"* (The brain is the organ where madness is born . . . Man becomes insane due to moistness of the brain, where functions of the soul are located). *"Cerebrum insanimus et deliramus . . . . Insania enim contingit, si cerebrum nimis humidum est."* (The brain makes us become mad and deliriant . . . . Madness ensues if the brain is excessively moist).

2. Caelius Aurelianus (203–249) strongly advised against the use of violence, chains and starvation on the insane, the three universal "remedies" used in his times. His suggestion of using "irritant injections in the ear" as a way to reach the meninges with medications when treating mental patients is most interesting.

3. The psychiatric conceptions of the great Avicenna (980–1037), the Persian "Prince of Physicians," could be summed up as follows: that mental disturbances are originated by morbid changes in the proportion and composition of the brain and are divided in alterations of the imagination and memory, and true psychoses (melancholia, mania, imbecility, and dementia). Anomalies of the anterior brain cause alterations in the faculty of perception, anomalies of the midbrain produce imbecility, anomalies of the fourth ventricle and its surroundings cause disturbances of the memory. He recommended cold aspersions, diet, derivatives, and bloodletting as therapy for mania, and derivatives and emetics as therapy for melancholia. Avenzoar (1113–1162) was the first to recommend cauterization of the head as somatotherapy for manic patients.

4. Arnaldo de Villanova (1235–1311?), the great medieval Spanish physician of kings and popes, established in his incunabulum *Practica medicinae Arnoldi de Villanova*, the relations between manic and melancholic states and menstrual disorders.

5. According to a great many historians, the first mental hospital created in History, was the Hospital de Nuestra Doña Santa María de los Inocentes or *Casa de Orates* in Valencia, Spain. Established in 1409 as a result of the preachings of Brother Juan Gilaberto Jofré in the time of King Martin I, it was converted into a general hospital in 1484. In this *Casa de Orates* the humanitarian principles of treatment of the insane were applied for the first time, anticipating Pinel by a few hundred years.

6. The Spanish philosopher Juan Luis Vives (1492–1540), teacher at Oxford and Louvain and self-exiled liberal in Bruges, accepted by some authors as the Father of Modern Psychology, represents the liberation of philosophic thought from the dogmatism of authority and the introduction of sound experimental criteria, as per his book the *Anima et Vita*, first of the great biological psychologies. He also defended the scientific and social functions of Psychiatry in his "Tratado del Socorro de los pobres" (1525). Vives, because of his splendid study of the passions, has been considered by many as the precursor of Freud.

BIBLIOGRAPHY

BAILEY, PERCIVAL: Cortex and Mind ("Midcentury Psychiatry"), Springfield, Charles C Thomas, 1953.

BOMFORD, R. R.: Changing concepts of health and disease with particular reference to "psychosomatic medicine," Brit. M. J. No. 4811, p. 633, (March) 1953.

CASTIGLIONI, ARTURO: A History of Medicine, New York, Knopf, 1947.

CAWADIAS: Clinical science in the light of history, Proc. Roy. Soc. Med. 40:453 (June) 1947.

CERLETTI, U.: "L'électrochoc," Rapports du Congrès International de Psychiatrie, IV. Thérapeutique biologique, 1950, p. 1.

COBB, STANLEY: One hundred years of progress in neurology, psychiatry and neurosurgery, Arch. Neurol. & Psychiat., p. 63, 1947.

DELGADO, HONORIO AND MONTALVO, PAZ: El Médico, la Medicina y el Alma, Madrid, 1952.

ENTRALGO, P. LAIN: La obra de Freud y el Cristianismo Primitivo, Revista de la Universidad de Madrid. 1: (No. 4) 1953.

ENTRALGO, P. LAIN: La Psiquiatría española en el siglo XIX,—in Vestigios, Madrid, Espasa, 1945.

GALDSTON, IAGO: Psychiatry in Medical History, in Modern Attitudes in Psychiatry, New York, Columbia Univ. Press, 1947.

GUTHRIE, DOUGLAS: A History of Medicine, New York, Lippincott, 1946.

MARTÍ-IBÁÑEZ, F.; SACKLER, A. M.; SACKLER, M. D.; SACKLER, R. R.; CO TUI, AND VAN OPHUIJSEN, H. W.: Neuroendocrinologic Basis for a Metabolic concept of several psychiatric disorders, Internat. Record of Med. 166:81 (March) 1953.

MIRA, EMILIO: Psiquiatría Clínica, Buenos Aires, El Ateneo., 1952.

NÁGERA, A. VALLEJO: Tratado de Psiquiatría, Barcelona, Salvat., 1949.

SCEOPUL, T. NICOLAS: Progresos terapéuticos en la Psiquiatría moderna, Prensa méd. argent. 38:694 (No. 12) 1951.

SIGERIST, HENRY E.: A History of Medicine, Oxford University Press, 1951.

ULLERSPERGER, VAN, J. B.: Die Geschichte der Psychologie und der Psychiatrik in Spanien, A. Stuber's, Buchhandlung, 1871. Translated into Spanish by V. Peset as "Historia de la Psicología y de la Psiquiatría en España," Madrid, Alhambra, 1954.

WHITBY, LIONEL: Progress and present aspects of medical science, Lancet. No. 6461: 895 (June 28) 1947.

ZILBOORG, G. AND HENRY, G. W.: History of Medical Psychology, New York, W. W. Norton, 1941.

Progress in psychiatry, Brit. M. J., No. 4644, p. 66, (Jan. 7) 1950.

Shock therapy, Psychiatric Bulletin, 1:38 (Spring) 1951.

Electroshock Therapy

Ugo Cerletti, M.D.

ROME, ITALY

THE DISCOVERY OF ELECTROSHOCK

In 1932, while director of the Neuropsychiatric Clinic in Genoa, I undertook some experimental research on epilepsy. A few years before that, as a pathologist in the Mombello Psychiatric Hospital in Milan, I had noticed in the autopsy of serious epilepsy cases the frequency of sclerosis in one particular convolution of the brain, namely, the cornu Ammonis, and, specifically, in one part of the same—the so-called Sommer's sector. I encountered this finding in approximately 50 per cent of the cases. It was a question as to whether the sclerosis or atrophy with induration was to be regarded as the cause of the epileptic syndrome, or was it likely that it is a consequence of the many convulsive attacks suffered by the patient? I resolved to explore experimentally this second possibility by subjecting dogs to numerous convulsive attacks over a long period and subsequently studying the brain alterations microscopically, particularly those in the Sommer's sector.

At that time many convulsivants were already available, but in order to avoid the possibility of cerebral alterations produced by the drugs themselves, we thought that it would be better to use purely physical means in such experiments, i.e., the passage of an electric current through the brain. And in view of the fact that the passage of an electric current through the brain several times might also produce some histologic alterations, I sought to avoid insofar as possible the application of electrodes to the head. The physiologist Viale, who had performed noteworthy experiments on fulguration, suggested that I might avoid the passage of the current through the head of the animals by applying one electrode in the mouth and the other in the rectum. We later found that even with this technic a part of the current reached the brain. Nevertheless, I used this means for some time to obtain typical epileptic convulsions.

In these experiments I observed that this so-called mouth to rectum circuit was dangerous. I was employing the 125 volts of electric current for varying lengths of time, and soon I realized that if the application time of the current was too long (by a few seconds) it induced the convulsions, but it often caused the death of the animals as well. Consequently, I had to shorten the application time. Using a common interruptor and a metronome, it was possible to perform serial applications of short duration—averaging one and a half seconds—with very few deaths. The histopathologic studies on the epileptized dogs had been preceded by careful description on the physiopathologic effects induced by the electric currents, and a paper was published by my assistant Chiauzzi[1] who, with Balduzzi and Lazzeri, had been collaborating in these experiments.

After a period of delay, the experiments were resumed in Rome (1935) in collaboration with Bini, and there we were able to collect a large amount of experimental material. While

we were preparing the histologic preparations, Bini[2] published the description of the epileptic seizures we had been inducing in our experimental dogs.

In the meantime, two new "biologic" treatments for certain psychoses had been proposed: the insulin coma by Sakel and the cardiazol shock by Meduna. In Vienna, I learned the therapeutic technic of insulin coma directly from Sakel, and I also sent my assistants, Accornero and Bini, to the Vienna Clinic. Then we introduced the application of this treatment to the Neuropsychiatric Clinic of the University of Rome. Longhi and I also began experimenting on human beings and animals with Meduna's method of using cardiazol intravenously.

Through the latter method, for the first time we were considering epileptic seizures not as a harmful and pernicious manifestation, but as a useful one in certain psychotic states. While performing my experiments on the induction of epileptic seizures in dogs, I never thought that these experiments would have any practical application. Cardiazol induced in dogs the same seizures that electricity does, and since it had been established that it was possible to produce these seizures in man with the use of cardiazol, it was natural to assume that electric current could be substituted for cardiazol. Bini, while in Munsingen, reporting on our experiments on dogs, and I, in Milan at the Congress on Insulin Treatments, both mentioned the "possibility," which at that time was only hypothetical, of using electricity to induce convulsions in man as they were then produced by cardiazol.[3, 4] This possibility was often discussed at our Institute and particularly when observing, after cardiazol injections, the painful reactions which shook fully conscious patients for over a minute—as a result most of them refused the subsequent treatments. However, the idea of submitting man to convulsant electric discharges was considered as utopian, barbaric, and dangerous: in everyone's mind was the spectre of the "electric chair." And I myself found in the literature on electrology reports of death in man caused by electric currents of lower voltage than that used on our experimental dogs.

Time went on without any further step on my part towards the application of electric current to man, but a chance occurrence led me in this direction.

THE INVENTION OF THE ELECTROSHOCK

Vanni informed me that at the slaughterhouse in Rome hogs were killed by electric current. Such information seemed to confirm my doubts regarding the danger of electric applications to man. I went to the slaughterhouse to observe this so-called "electric slaughtering," and I saw that the hogs were clamped at the temples with big metallic tongs which were hooked up to an electric current (125 volts). As soon as the hogs were clamped by the tongs, they fell unconscious, stiffened, then after a few seconds they were shaken by convulsions in the same way as our experimental dogs. During this period of unconsciousness (epileptic coma), the butcher stabbed and bled the animals without difficulty. Therefore, it was not true that the animals were killed by the electric current: the latter was used, at the suggestion of the Society for the Prevention of Cruelty to Animals, so that the hogs might be killed painlessly.

It occurred to me that the hogs of the slaughterhouse could furnish the most valuable

material for my experiments. And I conceived, moreover, the idea of reversing the former experimental procedure: while on dogs my aim had been the use of the minimal quantity of current capable of inducing the seizure without harm to the animal, I now decided to establish the time duration, voltage, and method of application that would be necessary to produce the death of the animal. Electric current would therefore be applied through the skull, in different directions, and through the trunk for several minutes. My first observation was that the animals rarely died, and then only when the duration of electric current was greatly prolonged. The most striking symptoms were obtained when the current flowed through the body and not through the head. The animals that received the severest treatment remained rigid during the flow of the electric current, then after a violent discharge they would collapse on their sides for a while, sometimes for several minutes, and finally they would attempt to rise. After many attempts of increasing efficiency, they would succeed in standing up and making a few hesitant steps until they were able to run away. These observations gave me convincing evidence of the harmlessness of few tenths of a second of application through the head of a 125-volt electric current, which was more than sufficient to insure a complete convulsive seizure.

At this point I felt we could venture to experiment on man, and I instructed my assistants to be on the alert for the selection of a suitable subject.

On April 15, 1938, the Police Commissioner of Rome sent a man to our Institute with the following note: "S. E., 39 years old, engineer, resident of Milan, was arrested at the railroad station while wandering about without a ticket on trains ready for departure. He does not appear to be in full possession of his mental faculties, and I am sending him to your hospital to be kept there under observation . . . ." The condition of the patient on April 18 was as follows: Lucid, well-oriented; deliorant ideas that he described with neologisms of being telepathically influenced with related sensorial disturbances; his mimicry is correlated to the meaning of his words; mood indifferent to environment, low affective reserves; physical and neurologic examination negative; presents conspicuous hypacusic and cataract in L. E. A diagnosis of schizophrenic syndrome was made based on his passive behavior, incoherence, low affective reserves, hallucinations, deliorant ideas of being influenced, neologisms.

This subject was chosen for the first experiment of induced electric convulsions in man. Two large electrodes were applied to the frontoparietal regions, and I decided to start cautiously with a low-intensity current of 80 volts for 1.5 seconds. As soon as the current was introduced, the patient reacted with a jolt and his body muscles stiffened; then he fell back on the bed without loss of consciousness. He started to sing abruptly at the top of his voice, then he quieted down.

Naturally, we, who were conducting the experiment, were under great emotional strain and felt that we had already taken quite a risk. Nevertheless, it was quite evident to all of us that we had been using a too low voltage. It was proposed that we should allow the patient to have some rest and repeat the experiment the next day. All at once, the patient, who evidently had been following our conversation, said clearly and solemnly, without his usual gibberish: "Not another one! It's deadly!"

I confess that such explicit admonition under such circumstances, and so emphatic and commanding, coming from a person whose enigmatic jargon had until then been very difficult to understand, shook my determination to carry on with the experiment. But it was

just this fear of yielding to a superstitious notion that caused me to make up my mind. The electrodes were applied again, and a 110-volt discharge was applied for 1.5 seconds.

We observed the same instantaneous, brief, generalized spasm, and soon after, the onset of the classic epileptic convulsion. We were all breathless during the tonic phase of the attack, and really overwhelmed during the apnea as we watched the cadaverous cyanosis of the patient's face; the apnea of the spontaneous epileptic convulsion is always impressive, but at that moment it seemed to all of us painfully interminable. Finally, with the first stertorous breathing and the first clonic spasm, the blood flowed better not only in the patient's vessels but also in our own. Thereupon we observed with the most intensely gratifying sensation the characteristic gradual awaking of the patient "by steps." He rose to sitting position and looked at us, calm and smiling, as though to inquire what we wanted of him. We asked: "What happened to you?" He answered: "I don't know. Maybe I was asleep." Thus occurred the first electrically produced convulsion in man, which I at once named "electroshock."

To complete the history of the first patient treated with electroshock, I must note that after eleven applications, the patient wrote the physician of the Institute on the following May 15 a well-composed letter in which he described his previous disturbances and treatments received and thanked the physicians for what they had done for him. We later received information from the Mombello Psychiatric Hospital (Milan), where he had been precedently treated, with the following report: "This patient was admitted for the second time in our hospital on December 28, 1937, at which time he presented auditory hallucinations and deliorant ideas of being influenced by means of machines, as well as of being persecuted, particularly by his wife. The case was diagnosed as paranoiac schizophrenia. He was treated with eight intravenous injections of cardiazol and showed some improvement. Thereupon he presented a condition of acute rheumatic fever which was cured in 18 days, after which he was released in his wife's care."

After this he came to Rome. He was discharged from our Institute on June 17, 1938, in good condition and well-orientated; ideation and memory perfect; he was critical of both his hallucinations and of his persecution ideas which he plainly related to his disease. While in our Institute, he was in correspondence with his family.

A year later, Professor Corberi of Milan reported that the patient was working regularly at his old job. The patient said that he was perfectly well; but his wife reported that three months after his return home he resumed his jealous attitude towards her, and that sometimes during the night he would speak as though in answer to voices.

At the first International Congress of Psychiatry (Paris, 1950), referring to the "invention" of electroshock, I declared: "It is plainly evident that the application to man of what we call electroshock was neither a discovery nor an invention. We shall call it a deed of courage, the courage of passing from the 'possibility' to the practical application. This is what I did. And I have assumed this heavy responsibility on the basis of my five years of experimentation on animals in Genoa and Rome and on my more recent experiments on hogs in which I established the dosage and maximal duration of the current."

In May, 1938, I described to the Medical Academy of Rome[5] the history of my research which, through the experiments on animals in Genoa and Rome, had led me to the application of electricity as a convulsant stimulus in man. I described the characteristic picture of electroshock; and, assisted by Bini, I gave a practical demonstration of an electric convulsion produced in a patient in comparison with a cardiazol convulsion produced in another patient. After my exposition, Bini provided information on the different mechanisms he had devised to regulate duration and intensity of the current.

DEVELOPMENT OF ELECTROSHOCK STUDIES

While the first practical therapeutic applications of the electroshock were in progress at our Institute, I realized that the electroshock offered a splendid method for physiopathologic and clinical research, because we had at our disposal, for the first time, the possibility of inducing *in man*, at will and without harm, the powerful reaction of the nervous system. We now had an invaluable method for investigating analytically and in progressive steps (with variations in dosage) the various phases of the epileptic attack, so that we would now be able to clarify its physiopathologic mechanism, to assay its biologic meaning, and particularly its therapeutic mechanism on the two psychoses, the manic-depressive and the schizophrenic, which we were starting to treat with the electroshock in a routine manner.

But before starting the practical applications of electroshock, it was necessary to clarify some basic problems with regard to safety of treatment. First it had to be established whether a series of electric convulsions could in any way damage either the brain or other parts of the organism; in fact, the already extensive experience with the other two methods of shock, the insulin and the cardiazol, seemed to indicate that good therapeutic results could be obtained only with several applications. Therefore, I started by expanding and increasing in a new series of animals the experiments previously performed in collaboration with Bini[6] on the anatomicopathologic modifications induced by electroshock in the brain in relation to varying voltages and frequency of electroshock applications.

The fundamental result of these experiments was that the electric current applied in the manner and dosage we had been planning to use in man, even after a series of twenty applications, would not induce any irreversible organic alteration in the brain. We observed only alterations of "acute type" in some nervous cells, particularly of the cortex and cerebellum, with diffuse distribution, and related reactive processes of the gray matter glia, partly of progressive type and partly regressive; moreover, we found slight regressive modifications in the small vessels. Altogether, the histopathologic picture can be compared to the one found in some subacute toxic states.

Dogs treated with a much greater number of applications (electroshock every five minutes for one hour or more) showed, in some parts of the cortex and in Purkinje's cells, many cells "with pyknotic retraction of the cytoplasm" (Nissl's stain). We judged that such retractions with condensation of the chromaffin substance resulted from the action of the fixative used (especially alcohol) upon a cytoplasm already swollen and softened by acute alteration (probably an edematous state).

This alteration, according to experimental hystopathology, is also reversible. We observed neither signs of "schwere Zellenerkrankung" (Nissl), which are destructive and irreversible, nor of the small focal productive alterations as observed by Accornero in animals subjected to several deep hypoglycemic shocks with insulin.

In a group of dogs that had been subjected several times to a prolonged action of the current (up to 50 seconds), we observed evident signs of tissular edema, these being acute alterations; in several cells the "schwere Zellenerkrankung" of Nissl, and many pericellular "incrusted spots;" fragmentation of cytoplasm and of cellular appendages; hyperchromasia, granules in the glia and in the perivascular spaces (Cerletti's perivascular corpuscles). Almost all were severe irreversible edematous-microbiotic lesions.

We never had the opportunity of studying these same histopathologic alterations in man for the reason that we never had any deaths among our patients treated with electroshock.

The above-described hystopathologic observations brought us to the conclusion that electroshock, within the limits we had established for its application, would not induce in the brain any serious or irreversible alteration.

As soon as electroshock became a routine therapeutic application for the patients of our Institute, I decided on a series of research projects to be carried out by my assistants with the aim of studying electroshock from a practical point of view. Bini[7] perfected the instrumentarium and analyzed the clinical manifestations of electroshock. Accornero[8] studied pulse, respiration, blood pressure, and temperature variations during electroshock. Laurenzi[9] investigated apnea and respiratory rhythm; Vattuone,[10] the deep reflexes; Felici,[11] the hematologic variations; Castellucci,[12] the glycemic curve; Bertoloni,[13] Donaggio's "obstruction phenomenon;" Ciotola,[14] the retinal circulation and the crystalline reaction; Ferreri,[15] the vestibular nystagmus; Flescher,[16] the retrograde amnesia; Longhi,[17] the pathogenesis of epileptic manifestations; Challiol,[18] the influence of Luminal on the electroshock crisis; Rizzo,[19] the reproduction of convulsions by conditioned reflexes; and finally, Bini and Puddu[20] engaged in experimental research on the physiopathology of the cardiovascular and respiratory system during electroshock.

I, for my part, investigated the problems connected with the physiopathology of convulsive seizure in man, with a view to the possibility of dissociating the epileptic attack in its various phases through the use of different dosages of the intensity and duration of the stimulus, so that I would be able to analyze the mechanism of the attack. In such studies, I tried to resolve the phenomenon of loss of consciousness and the apnea and neurovegetative symptoms appearing with it. Later on I applied myself to the study of the duration and modality of the convulsive phase, with the aim of explaining the mechanism of the attack. Also, I investigated, by measuring the pressure of the C.S.F., the possibility of angiospasm as the inducing cause of the convulsive attack.[21] Then I did some research on the biologic significance of the convulsive attack. Finally, I decided to face the complex problem of the therapeutic mechanism of electroshock in manic–depressive and schizophrenic psychoses, which were the first two diseases to be treated in our Institute.

All the studies and research projects carried out by my assistants and myself were published in a special issue of the *Rivista Sperimentale di Frenatria* in 1940.

THE TECHNIC

My point of view has always been that electroshock is not an electric treatment, but a convulsant treatment. Meduna was the first to show the benefits of an induced convulsion (with cardiazol) in some mental diseases. I formerly considered the electricity as merely one of the many stimuli, either physical or chemical, capable of inducing a convulsive attack. But as I soon observed, and as has been subsequently recognized by many other workers, electric stimulus has been shown to be most suitable:

(1) because the subject does not have time to sense it, and the attack develops while he is completely unconscious;
(2) it causes a retrograde amnesia, so that the patient does not remember, and he believes he was sleeping throughout the application. He, therefore, offers no opposition to the subsequent applications;
(3) the convulsion is not so violent as with the other methods, so that accidents rarely occur;

(4) post-convulsive reactions from psychomotor stimulation are rare. Convulsive consequences have never been reported.
(5) electroshock can be repeated without harm at the same sitting;
(6) intensity of stimulus can be modified to obtain lesser reaction;
(7) application is of short duration;
(8) cost of electroshock is low.

The simple instrumentarium I first used in Genoa was subsequently perfected by Bini: he added a stopclock of the same type used with roentgen machines to measure the duration of the current; an electromagnetic voltameter to measure the current tension; and tonglike electrodes with specially designed movable supports.

The first "official" machine (Arcioni, 1940) was equipped with a complicated device that was supposed to measure the electric resistance of the head of the subject, with the object of thereby regulating the minimal quantity of current needed to induce the shock. Later this device was discarded, due to the difficulty of obtaining accurate measure of head resistance. The later machines, equipped by Bini, were consequently simpler and had only a switch-clock and a voltameter. The headcap was also replaced by two independent electrodes with handles and the time-regulating device, the voltameter, and the interruptor devices were located in the handles.

Bini's achievement in equipping this machine with so many safeguards for the operator to control the dosage (time and voltage) has been a contributing factor to the expansion of electroshock all over the world.

Of course, there were soon on the market many modifications and improvements of the first machines. These modifications were first introduced with the aim of reducing the degree of the electric spasm, i.e., the abrupt and violent contraction of all muscles during the very brief duration—fraction of seconds—of the flow of the current. This electric spasm was blamed for the unpleasant accidents which sometimes occurred in the application of electroshock, i.e., dislocations and fractures. I believe that dislocations and fractures (which rarely occurred) are also produced—perhaps even oftener—during the tonic and clonic phase of the convulsive attack. In fact, in the "epileptic absentia," which also shows the "electric spasm," but without convulsions, we have never observed such accidents.

I have always maintained that in the therapeutic mechanism of electroshock the electricity itself is of little importance: it is only an epileptogenic stimulus, while the important and fundamental factor is the convulsion, no matter how it is obtained. Therefore, maintaining that only the convulsive attack induced with the minimum stimulus is the essential therapeutic factor, I have never paid much attention to the different variations of the electric machine proposed. As I said before, Bini himself simplified his first machine. Felici,[22] another assistant of mine, while Director of the Psychiatric Hospital in Tripoli, used electroshock during the last war and also performed interesting research by employing the minimum instrumentarium: he would simply insert the plug rapidly and for a fraction of time of about five tenths of a second in a regular current outlet (150 volts).

Nevertheless, I have always followed with great interest the different modifications introduced in the electroshock machine; but I do not believe it necessary to go further in dis-

cussing the subject or the various electric treatments which include the so-called "electric stimulations" of the brain.

At the International Congress of Psychiatry (Paris, 1950) I[23, 24] offered a long list of the different electric instrumentaria proposed by various authors, but I then concluded that only a wide experience in the practical application of electroshock could establish which was the best technic to employ for maximum therapeutic advantages and optimum methods of application. After four years, while not doubting the good results obtained by some workers, it is my impression that the great majority of physicians are still following the original convulsant method I proposed. In another part of this paper we shall discuss why the immediate induction of a complete epileptic convulsion is to be preferred to the induction of attenuated reactions by electric stimulation of the brain, ranging from the various forms of "absentia" to the so-called "electronarcosis."

In what part of the brain and in what manner the electric stimulus acts to induce the attack is an unresolved problem. Bini, in 1940, showed that in dogs (healthy and with the thorax open) an electric current flowing through the head also spreads in minimal amounts (milliampere fractions) through the thorax and abdomen. Wagner, Smitt, and Wagener observed that the 90 per cent to 95 per cent of the total voltage does not reach the brain but is lost in the skin and in the gales. My assistant, Bollea, and, the electrotechnician, Dr. Manfred[25] established by experiments on dogs and man (postmortem and *in vivo*) that the ratio of resistance of the C.S.F. and cerebral substance is 1 to 16, for which reason the cerebral fluid is of great importance in the distribution of electric current through the encephalic mass. The maximal intensity of the current was recorded in the basal and interhemispheric periventricular zones.

NEUROLOGIC SYMPTOMATOLOGY OF ELECTROSHOCK IN MAN

In any individual, the flow of an electric alternating current of about 125 volts through the head for two tenths of a second will induce a pure epileptiform attack. This is preceded by a peculiar reaction to the electric stimulus, a reaction which lasts exactly for the duration of the current flow, i.e., two tenths of a second, and which consists of a sudden contraction of the whole musculature, with the trunk in opisthotonus and the limbs in extension. Heart and respiration are briefly arrested; pupillary reflexes are present. Above 300 ma. there is also a momentary clouding of consciousness; but immediately thereafter the patient shows some intentional movements, and he may even mutter a few words. We have called these reactions "electric spasm," which is still not the true epileptiform attack. Between the electric spasm and the true attack there is always a short pause of from one half second to 10 to 30 seconds, so that the epileptiform attack which follows cannot be assumed to be a nervous reaction correlated to the flow of the current. Every individual has the complicated phenomenic constellation of the convulsive attack already preformed in his brain and ready for the discharge: when an adequate stimulus, in this case an electric one, overcomes the threshold, we have an epileptic discharge, just as a big mine is made to explode by a small detonator. The explosion, or rather the attack, is usually very uniform, constant and pure, at least in brains that are anatomically sound. In epileptic patients, the convulsive attacks

show many variations due to the presence of gross anatomic alterations in the brain. In healthy brains, we can observe slight variations in the electroshock only during the post-convulsive recovery phase, and these depend on individual constitutional differences.

For the understanding of the therapeutic mechanism of electroshock, I felt it necessary to increase our knowledge of the convulsive attack itself. In view of the fact that we were able to induce in human subjects a series of uniform attacks, and that we were able to subdivide the attacks in its various phases by graduation of the intensity and the duration of the current flow, the electroshock seemed the ideal method for an analytic examination of the convulsive attack.

Its complex and precipitating symptoms must be divided into basic and secondary. For many years we had found quite satisfactory Kroll's[26] definition of the epileptic syndrome which he describes as "characterized by loss of consciousness, *accompanied* by several pyramidal and extrapyramidal vegetative disturbances, of which the most conspicuous are the tonic-clonic contractions." From clinical cases we learned that the accompanying and most conspicuous phenomena of the epileptic attack, namely, the motor symptoms (pyramidal and extrapyramidal), are not the essential phenomena of the attack. For example, the many cases of "petit mal." And in regard to the vegetative phenomena, which Kroll lists among the less important, our studies have demonstrated that they are essential and appear to be the substantial core of the attack.

ESSENTIAL REACTIONS

(1) Loss of consciousness. Summarizing my studies during 1940, 1946, and 1950: Besides the different varieties, or levels, of consciousness, namely: gnoseoconsciousness (intelligence, knowledge, elaboration), and thymoconsciousness (instincts, emotivity, affections), there is a more primordial form of consciousness which gives in man, and probably also in animals, the general sensation of being alive in relation to his external and internal environment (ontoconsciousness, cenestoconsciousness). This is the primordial psychism through which simple defense reflexes develop, and also conditioned reflexes, after repeated adjustments to new situations and events. This primordial, or simply "vigilant," consciousness has also been called "vegetative." It rules the organic body and represents the core of the organism (Kuppers,[27] Hascovec,[28] Camus,[29] Hess,[30] Kleist,[31] etc.).

While the cerebral cortex presides over the more elaborate manifestations of the consciousness, we agree with the majority of authors that this elementary level, this so-called "commutator" of somatobiologic processes, (the consciousness being restricted to a vigilant or watching state, in contrast to the sleeping state) is localized in the hypothalamic-diencephalic formations (Rohrbacher,[32] Gamper,[33] Kornmueller, Duret;[34] Berner and Neubuerger;[35] Redlich,[36] Strauss,[37] Kamper,[38] etc.).

The inhibitory block of this neurovegetative center produces a massive blackout of the consciousness, a deep coma. But unlike the other known comas, in which the breathing is conserved, it is accompanied by another phenomenon of neurovegetative block, i.e., by apnea.

(2) The apnea is also an essential reaction of the convulsive attack, so that we observe it

in the "absentia epileptica." Here we do not have the respiratory muscles fixed as in the tonic phase of the complete epileptic attack. Moreover, according to my research, the apnea by electroshock is observed also in subjects anesthetized with ether and in a state of total muscular relaxation. Therefore, we must consider the apnea as a phenomenon of central origin. There is some doubt whether the apnea is due to a direct inhibition of bulbar respiratory centers or whether these centers are blocked by an inhibitory stimulus from the respiratory diencephalic preinfundibular centers (Boon's group B).[39] The latter mechanism is the most probable: (A) due to diffusion of the stimulus of the contiguous diencephalic centers that block the consciousness; (B) because other hypothalamic formations are involved; and (C) because even the most violent epileptic attacks never endanger life, and this can be more easily related to perturbations of the hypothalamic centers, nonessential for life, than to any direct damage of bulbar centers.

Besides these two essential phenomena—loss of consciousness and apnea—there is a series of other phenomena also depending upon the neurovegetative diencephalic system; these phenomena are essential because they set in during total and partial seizures. We will only mention them here. We have already discussed (1) loss of consciousness and (2) apnea. The latter lasts for 40 to 60 seconds, then breathing starts as a movement of deglutition which is soon after replaced by the characteristic stertorous respiration. (3) Together with the foregoing, we observed the following symptoms: pallor during the first few seconds, followed by congestion of the face; then, after about one minute there was pallor followed by cyanosis. (4) After a very brief stoppage of the heart, it again starts to beat with a vagal rhythm for about one minute, then there follows a tachycardia lasting an average of two minutes. (5) First there is hypotension, then hypertension for about two minutes. (6) Mydriasis and pupillary rigidity for one minute, then myosis. After one and half minutes, there is a paradox reaction for about 30 seconds—(7) Weeping, sweating, salivation. (8) Gooseflesh during the first minute. (9) Sometimes erection, ejaculation; rarely micturition, loss of feces. (10) Hypoglycemia in the first two minutes; then hyperglycemia.

These and other minor constant manifestations of the convulsive attack were studied by me and by my assistants in 1940, and since then we have been studying their mechanism of action and their anatomicophysiologic localization. It appeared that they should be considered as originating from the hypothalamic-diencephalic formations, as by direct stimulation of the hypothalamus which was demonstrated by Karplus and Kreidl[40] and subsequently by other workers. The research since then by Castellucci[12] on glycemia and by Felici[11] on hematologic modifications has been progressively enlarged and completed by many studies on the humoral syndrome of electroshock.

We owe particularly to Delay, Soulairac,[41] et al a large series of observations that have contributed new and invaluable data and a better understanding of this humoral syndrome. These workers first set out to determine the humoral displacements induced by the complete electric attack: hyperglycemia, hyperlipemia, hyperproteinemia, hypercalcemia, hypopotassamia, acidosis, hyperchloremia, hypernatremia, hyperphosphoremia, oliguria with hyperconcentration of urea, chlorides and phosphates, hyperglycorrhachia and hyperleucocytosis; then they performed a comparative series of research experiments on electroabsentiae with the object of determining which modifications refer to the muscular stress (during the tonic-clonic phases), and they were able to establish

that hypercalcemia, hypopotassemia, hyperproteinemia, acidosis, and hematic concentration in particular were related to such stress.

All the other humoral displacements are to be attributed to diencephalic functions.

A series of experimental researches conducted in our Institute produced in negative form the same results obtained by Karplus and Kreidl by the direct stimulation of the hypothalamus. Longhi and Martinotti (1946–1951)[42] were able to exclude the influence of the mesodiencephalic formations in rabbits by summation (12 to 15 electroshocks at two minute intervals).

With such "summation syndrome" we are able to induce: (1) insufficiency of the thermoregulating mechanism; (2) lack of temperature increase with injection of vaccines; (3) a steep rise followed by a sharp decrease of the glycemic curve after glucose injection intravenously, which indicates a bulbar type of glycemic regulation in dependence of diencephalic control release; (5) intravenous injection of pentothal hinders recovery, upright position, and deambulation: these were present in control animals after eight minutes, but only after 25 to 30 minutes in treated animals.

Retention of chlorides in electroshock summation by rabbits was seen by Arduini and Bondolfi;[43] in their opinion diencephalic "centers" are functionally depleted of energy.

Much remains to be done in hormone research. In my experiments, histologic changes in glands of pigs that were shocked (15 shocks, given every second day) may be summarized as follows: Hypophysis: hyperemia; increase in eosinophilic cells; absence of basophilic cells (Merucci).[44] Adrenals: hyperemia. Lipids are no longer seen in the cortical layer (Merucci).[44] Thyroid: Basedowoid changes. Some follicles are bigger, some smaller than normal, and without colloid substance. Pluristratified epithelium, with thick cylindrical cells (Merucci,[44] Verdozzi[45]). It might be recalled that electroshock produces increased B.M.R. (Pero), increased blood pressure, and increased glucose in blood (Dogliani).

Damage of the thyroid as produced by thioureids in rabbits is prevented or lessened by electroshock (Delay et Soulhairac,[46, 47] De Gaetani). It is known that thioureids interfere with the hypophysis, the outmit of thyrotropic hormone being reduced. Thyroid hyperactivity produced by electroshock might be due to the increase of thyrotropic hormone. Hystologic evidence showed that interference with the thyroid gland is relevant in this organic reaction pattern, no matter what mechanism by which electroshock influences the thyroid gland.[41]

Therefore, what I maintained in 1940, by other means as well, namely, that the anatomicofunctional substratum of the vegetative syndrome induced by electroshock is to be localized in the diencephalic section of the cerebrospinal axis.

NONESSENTIAL MOTOR REACTIONS

Besides the neurovegetative reactions, which we consider essential, there are some nonessential motor reactions; in fact, in epilepsy, the complete attack—that is with convulsions—is observed only in 50 per cent of the cases. In the other cases absentia or equivalents we do not observe such a typical motor reactions. By the electroshock with reductions of volt-

age and variations of time, we obtain different kinds of "absentiae," viz., loss of consciousness and a neurovegetative syndrome.

The convulsions, which have always attracted the particular attention of physicians, cannot be explained as the result of the "discharge" of neurophysiologic levels of the neuroaxis. In the convulsions we see neither the classic discharge's hyperkinesis nor the decerebration symptomatology. Not even the tonic phase can be identified as a discharge hypertonia (Moruzzi[44]). The latter states that the tonic contraction is a very violent contraction similar to the strychninic or tetanic contraction. On the contrary, the clonic contractions can be interpreted as originating from exhaustion pauses of the excessive muscular contraction.

Longhi[42] has investigated by means of electroshock summation in rabbits the exhaustion of the centers which presumably preside over these motor discharges: he observed that with an increasing number of applications (one every two minutes) the tonic-clonic syndrome would become progressively weaker until it completely disappeared, after 12 to 15 electroshock applications in rabbits. In dogs, after 35 to 40 electroshocks, once the brief "electric spasm" is over, the recovery is rapid without other convulsions: the dogs are disoriented and run around the room, avoiding obstacles by a glimmer of consciousness. In rabbits we observe unusual posture of the limbs, opisthotonus of the head and trunk, retroflexion, and retropulsion, reinforcement of the tonic reflexes of the head upon the limbs. The normal chronaximetric ratio between flexors and extensors of 1:2 becomes 1:1. These findings are evidence, for the motor field, of the functional impairment of the mesencephalic centers.

But the motor syndrome of the epileptic attack is not limited simply to tonic-clonic reactions. We have defined here some features of the motor syndrome which characterize it very distinctly. Firstly, we observe the contractions of the mimic muscles, and the consequent expression of terror; then the opening wide of the mouth and the outcry, which is not the result of deep expiration with closed glottis, and often is frightful to hear; the powerful trismus, appearing after 30 seconds and remaining present without any relaxation during all the phases of the motor attack: the tonic, clonic, and relaxation stages. In the latter stage useless automatic movements may appear; then with the gradual regression of consciousness we observe, little by little, a purposeful motor activity, i.e., fetal position of sleeping, rubbing of the face, carpology, attempts to escape. Later on, rough movements set in; finally the fully conscious and voluntary motility appears.

BIOLOGIC SIGNIFICANCE OF THE CONVULSIVE ATTACK

The analysis of the various manifestations of the convulsive attack, of its clinical picture, or of its anatomicophysiologic mechanism, or of the interrelation of the different phenomena, is unsatisfactory in the end, because there is little evidence as to the significance, the value, and the importance of such a peculiar phenomenic constellation, which is indeed the greatest nervous reaction known. And every time that we watch its uniform and, so to speak, harmonious development, we ask ourselves how and why such a typical phenomenic constellation arises in the nervous system.

However, if we carefully follow it in man we can detect, in the first stage, some features

that suggest a functional interpretation. After the abrupt "electric spasm," the true attack generally starts with the tonic tension of the trunk and limbs, that assume either a defending or a repelling posture; but specifically, it starts with a typical attitude of the facial mimic that clearly expresses a state of terror. This interpretation is supported by the evidence of correlated symptoms—the initial outcry; vasomotor phenomena; pallor and congestion; sweating; mydriasis and pupillary rigidity; apnea, etc. This syndrome agrees in many points with the well-known "terrific syndrome" which has been described by many researchers including Darwin and later, in a more "neurologic" way, Kroll,[26] Cannon,[45] Bard,[46] Rosenbluth, etc. This syndrome is characterized by deep perturbation of the consciousness, an expression of astonishment; dilated pupils; holding the breath; either deep pallor or congestion of the face; vagotonia; akinesia with muscular rigidity then with rapid, intense tremors, sometimes ending in true convulsions. In regard to the biochemical modifications, an interesting comparison was made by Delay between the humoral reaction of diencephalic origin observed with the electroshock, and the same humoral syndrome described by Cannon and Bard as diencephalic response to emotional shock.

Such a similarity of symptomatology between the first phase of the electroshock attack and the aforementioned "terrific syndrome" reaction shows that it is not simply for the sake of an oversimplified analogic interpretation that we have ascribed to the first phase of the electroshock attack the same significance as an unconscious "terrific syndrome" reaction. Still another point of evidence that we have is in the common phenomenon of the "after fear." I have already described[47] the "after fear" which we observe in many subjects following a few applications of electroshock: they hate to continue the treatment and regard it with a dismayed sensation of fear. This is a confused "organic" remembrance of the unconscious crisis of terror. Moreover, in our experimental researches with different animals we noted some differences, in comparison with man, in the picture of the electroshock attack, that were characteristic for each species. I therefore decided to enlarge and extend our studies of the electroshock attack by experimenting upon animals of different species including those phylogenetically far remote from man.

In collaboration with Longhi and Martinotti,[48] I recorded our observations in a motion picture that was filmed in the laboratories of the Superior Institute of Health, in the Prov. Psychiatric Hospital, and at the zoologic garden in Rome. We have already presented a preliminary showing of this moving picture at the First International Congress of Psychiatry in Paris.

We did not have in any species a picture of the convulsive attack with complete clearcut functional significance and, therefore, we have had to collect the most typical signs observed in each species.

In man, as already stated, the terror phase is the most evident. The same is also evident in dogs: the latter show, in the first phase, while unconscious, ruffled fur, grinding, bared teeth, and mydriasis. The syndrome is even more evident in cats. These show, as I described in 1925,[49] mydriasis and pupillary rigidity, teeth grinding, puffing of breath, flattened ears, and ruffled fur especially of the tail: i.e., the well-known picture of the cat terrified by a dog. This happens while the cat is in a state of unconsciousness; then the clonic phase

follows. Birds in the first phase tilt their head backwards, often hiding it under one of the wings. The aquatic birds dive deeply in water.

The second phase of the convulsive attack—the clonic phase—does not yield, in man and monkey, clear functional interpretations. On the other hand, it is very significant and characteristic in many animals, and we can easily synthetize it as a defense action which is typified by unconscious escaping movements. In dogs, the clonic phase is released in form of unrestrained running; in rabbits and cats, which are animals with strong hind legs, we observe violent movements of the posterior limbs as if they were trying to jump, though lying on the floor. In the hog, as in the case of sheep, we observe a typical gallop. In the gallinaceous birds, first there is a swift flutter, like an attempt to fly, then rhythmic, rapid movements of the legs as though attempting to run. In the stork, the clonic phase shows a slow rhythmic flutter, the same as in their characteristic flight, and, also, they hold their long legs steady, backward and joined together, as they do in their natural flight.

I will omit further detailed observations made in other animals, but there is no doubt that the clonic phase expresses, at least in many species, a motor complex of escape, i.e., a defense reaction. This does not appear clearly in men and apes, but they show a typical phenomenon which we believe exhibits the same defensive significance, i.e., trismus. Soon after the beginning of the tonic phase, the mandibular muscles are fixed by a strong contraction which does not follow the different phases that the other muscles go through, but remains even when the convulsive attack has passed to the relaxation phase.

I have studied also the grasp reflex during electroshock attacks: that of the hand appears only during the stage of transition from deep coma to the beginning of consciousness. Holding reflexes have also been observed at the cephalic extremity (for instance the "bulldog reflex" of Janischewsky): but, as demonstrated by Rabiner, even such reflexes as these call for a minimum of consciousness. On the contrary, the trismus of the epileptic attack sets in from the beginning of the attack and with complete unconsciousness. It is an elementary defensive-aggressive reaction that is prolonged unvaried for more than three minutes, including the relaxation phase, and which only with the slow return to consciousness assumes the character of a reflex; for when we try to pull the rubber mouth gag out of the mouth, we feel a strengthening of the mandibular squeeze.

The whole of the foregoing observations show that it is extremely probable that the convulsive attack represents a typical powerful reaction of terror and defense against definite stimuli that endanger the life of the individual.

Considering the convulsive attack as a complex reaction preformed in the neuraxis with the obvious significance of a final defense of the organism against a given harmful situation, we believe that once such a reaction has been induced by whatever method available (we have seen why the electric stimulus appears to be the most suitable) one should allow the reaction to proceed normally in its entirety.

The term electroshock should be restricted to this *natural* genuine reaction. But, with the application of electric stimuli of varied intensity and duration, the reaction has been variously modified. Consequently, the tonic phase has been shortened or lengthened, by inducing it gradually, and has been lessened in its intensity; the clonic phase, as done in the

various technic of "gliding," has been shortened and nearly abolished. With other technics, such as have been carried out with the various methods of "electronarcosis," the tonic phase has been prolonged and the clonic phase greatly reduced. In all the technics mentioned, an electric stimulus of varying strength is allowed to flow either during a part or during the whole of the attack.

Do we know exactly what happens in the cerebral tissue during such superposition of the organic discharge and of the electric stimulus? Do we have positive and definitive histopathologic observations in such a matter? Do we know how the neurovegetative-humoral syndrome is modified by such a crossing of stimuli and of discharges?

We are inclined, out of a sense of deference towards the very old defense mechanisms provided by nature all through the phylogenesis of organisms, to attribute to the complete, genuine convulsive attack the maximum of efficiency and harmlessness.

It may be that the other technics of electric application will attain unexpected therapeutic results; this we will not deny, but up till now there has been neither positive nor unanimous observations on this subject.

However, considering that with the use of the above-mentioned technics not only the natural organic reactions but also prolonged electric stimulations come into play, it is not proper to speak simply of convulsant treatments (electroshocks); rather, they should be called *electric treatments*, which in my opinion do not belong to the electroshock field. Even the use of weaker currents and shorter duration to reduce the attack at the plain "absentia" has for the large part been unsuccessful; and Delay and Soulairac have shown that in such minimized attacks of "petit mal," even if the humoral displacements due to the violent muscular contractions are eliminated (to any advantage), the diencephalic humoral syndrome is likewise also reduced. Other means, too, which have been employed to modify the natural discharge, whether by curarization or by narcotics or by anesthetics, have not been met with unreserved acceptance, not only because of many technical difficulties, but particularly because the therapeutic results have not always been satisfactory.

DEVELOPMENT AND PRACTICAL APPLICATIONS OF THE BIOLOGIC CONCEPT OF ELECTROSHOCK

Should we, then, continue to apply electroshock, despite its undeniable disadvantages, which, however harmless our experience has shown them to be, are none the less real? In such a matter, the scientific researcher has much the same philosophy as the explorer, who, having reached one coveted goal, follows the urge that may be summed up in the motto, *Et ultra!* (Onward!).

It was not long after I had first witnessed electrically produced convulsions in man and had confirmed that they had a practical application that I came to the conclusion that we must get away from the use of electroshock. When subjecting unconscious patients to such an extremely violent reaction as these convulsions, I had a sense of illicitness and felt as though I had somehow betrayed these patients.

With this objective in mind, namely, to find something that could take the place of convulsions, I spent a number of years in thorough study of convulsions—analyzing their com-

ponent elements including the reciprocal articulation of these elements, their biologic significance, and the therapeutic mechanism of the whole.

A convulsive attack may be divided into two phases—the tonic, or "terrific" phase, and a clonic, defensive phase. The terrific phase leaves an impression on the subconscious which later re-emerges in the characteristic "posthumous fear."

In my analysis of the mechanism of electroshock action, I found that the beneficial effects resulted not so much from the muscular spasms as from the profound neurovegetative, humoral, and hormonal modifications that are brought about in the course of the attack. I maintain, however, that the optimum results are achieved by allowing the attack to proceed undisturbed through all its phases.

I consequently came to the conclusion, as early as 1940, that electroshock produces the maximum defensive discharge of which the organism is capable, as a result of which the organism brings into violent play all the elementary biochemical nervous reactions especially regulated by the diencephalic neurovegetative system . . . reactions which, phylogenetically, were organized for the safeguarding and defense of life.

In my study of the therapeutic mechanism of electroshock in the two great "unclassifiable" psychoses, the manic-depressive and the schizophrenic, in which the first beneficial effects of the method were observed, I noted[21] one feature which was common to both diseases, involving major dysfunctions of those parts of the brain (hypothalamus-diencephalon) that preside over the instinctive-emotive-affective functions, or in other words, in disturbances of an opposite nature, and this was: (a) in excess: manifestations of hyperthymia (in melancholia, sad hyperthymia; in mania, gay hyperthymia); and (b) in deficiency: athymia or hypothymia (in schizophrenia*). I concluded that the therapeutic action in the two above-mentioned psychoses had to be attributed "to the violent activation of the elementary, vital defense processes, as the reserve reactions as a whole which lie latent in the nervous system and the entire organism may rightfully be called." Naturally, these reactions are quicker and more efficient in a brain which is excessively vibrant with manifestations of hyperthymia, as in a manic-depressive psychosis, than in a brain which is somnolent and blocked with "athymia," as in the case of schizophrenia.

From this I deduced a working hypothesis that can be summed up as follows: to demon-

* For many years I have maintained that, when one is undertaking to arrive at the basic, or better said, *primitive*, disturbance responsible for schizophrenia, it is more important to take into account the disaffective phenomena, i.e., the abolition of the instinctive-emotive-affective functions (athymia, hypothymia) than the dissociative phenomena. This is clearly evident in the early stage of schizophrenia. Dissociation appears later and is found in patients already hospitalized for some time, as a consequence of athymia. The lack of an incentive or purpose or of any affective commitment to serve as a guide to thought and action gives rise to vacuity of thought, ideational misery, and difficulty in performing any conclusive, efficient act, as well as to the inability to distinguish fugitive thoughts from important ones, or to retain ideas in accordance with their value. Hence, the dispersion of thought, blockage, dissociation, and the disagreeable sensation of being the victim of strange forces, which in turn give rise to vague ideas of being subjected to influences and of persecution, and later, to pseudohallucinations. The absence of instinctive-affective tonus eliminates the urge to act and results in the characteristic aimless, unmotivated and incoherent behavior of the schizophrenic.

strate, if possible, the formation in the organism, under the influence of electroshock, of defensive substances.

As early as 1945, Doussinet and Jacob[51] experimented by injecting mental patients intravenously with plasma and serum taken from other patients who had been subjected to electroshock. They observed palliative effects in "negativistic patients" and in those with anxieties. To me, this use of serum from other psychotic patients did not appear to prove much, and, in view of the great complexity of the reactions set in motion throughout the entire organism by electroshock, and the complex counterreactions of the various tissues and glands of internal secretion, it seemed more appropriate to aim directly at the organ with which electroshock is primarily concerned, namely, the *normal* brain—using animals that had been previously subjected to electroshock.

I experimented with a number of different animals, and, for various practical reasons I decided on pigs, because they are able to stand up quite well even under a quite extensive series of electroshocks, and they have a highly developed brain that has a comparatively substantial weight (a little over 100 Gm.).

In order to minimize changes in the cerebral substance I discarded extracts and prepared the brain *in toto* in aqueous suspension, in the manner customarily followed in the preparation of antirabic vaccine.*

Since the substance derived was later to be injected in patients, the delicate question arose of the toxicity of these *in toto* suspensions of a heterogenic brain. I studied the extensive literature on the subject and, in particular, the records of the vast experience accumulated over a long period with antirabic treatments, in which symptoms of encephalitis have been encountered only in the most exceptional instances and these for the large part of a benignant nature.

Accordingly, I had Bonfiglio, Jr., and other physicians attached to the Clinic and to the Psychiatric Hospital of Rome undertake preliminary experiments on man with intramuscular injections of brain suspensions from normal and electroshocked pigs, after studying the general condition, blood, and fluid of the subjects, which were negative in every case. The first series of experiments was carried out on patients who, as is well known, derive the maximum benefit from electroshock, namely, manic-depressive endogenous hyperthymia cases. Injections of a 10 per cent aqueous suspension of normal pig brain (with 1 per cent carbolic acid) were given daily for eight days in a dosage of 5 to 10 cc., and subsequently, for 10 to 15 days, of a suspension of the brains of pigs previously subjected to varying degrees of electroshock (from 7 to 42 electroshocks, once daily).

The results, which were wholly negative in the case of the normal pig brain, were, on the contrary, highly interesting in the cases where electroshocked brain was used. In 24 of 36 patients, insomnia shortly disappeared—insomnia being, as is known, a constant feature of endogenous hyperthymia. Some patients became somnolent within a half hour after

* This research project was carried out over a period of years at the Clinic for Nervous and Mental Disorders of the University of Rome, and in the laboratories of the Istituto Superiore di Sanità. The chief expenses were borne, for the large part, by the National Research Council (Consiglio Nazionale delle Ricerche).

the injection. In one case, after three days of treatment, the patient fell into a tranquil sleep which lasted four days with normal possibility of reawakening. With suspension of the injections, this continuous sleep ceased. In 27 of the 36 cases, a remarkable change of disposition toward the normal was noted. In 16 of 18 patients with anxieties, there was a notable attenuation of the anxiety state; while in 4 hypomaniacs, who had received larger doses, complete suspension of excitation resulted.

Typical reactions of the neurovegetative system were also observed, such as flushed face and profuse sweating. In some cases there were slight increases in temperature (99 F. to 100 F.). In regard to improvement of appetite and the general state of nutrition: after 20 days of treatment, one patient showed a gain in weight of 4 pounds 6½ ounces, while another showed a gain of 8 pounds and 13 ounces.

Of the 36 patients, 12 were cured after a treatment of 20 injections; 16 showed decided improvement; and 8 presented no change (the average doses given proved later to have been low). This first test series had no clinical objective but was solely for scientific purposes: what I wanted to demonstrate was the existence of differences in the properties of electroshocked and unelectroshocked cerebral substance.

The above-described results were certainly encouraging, but they were not decisive. Although endogenous hyperthymia cases can be considered an integral group from the physiopathologic point of view, they may not be considered so from the etiopathogenic viewpoint. The stages of the illness vary from case to case; symptoms being variable.

I therefore sought to find a biologic test which would be more clearcut and decisive, and for this purpose I chose a serious disease with a constant course and a uniform outcome (death) within a fixed period, i.e., rabic encephalitis in rabbits, to be induced by intracerebral inoculation of the so-called fixed virus.

Due to postwar difficulties and the epidemic wave of toxoplasmosis in rabbits, the first experiment had to be restricted to a limited number of animals. Twenty healthy rabbits (as indicated by negative fluid) were treated for 24 days with 1.5 cc. injections of a suspension of electroshocked pig brain, and a second group with injections of a suspension of normal pig brain. A third group had four preventive electroshocks and four after the fixed-virus inoculation. A fourth group served as a control group. After this varying preparation, all were inoculated intracerebrally with the fixed virus of rabies. The rabbits of the last three groups, with an absolutely uniform reaction, were apparently normal for six days. Thereupon, for 24 hours, they presented paretic-ataxic phenomena. Finally, for two and a half to three days, they fell into a profound coma that ended in death. However, of the rabbits that had received preventive treatment with electroshocked brain, 2 showed a prolongation of the incubation period by one to three days; a shortened paretic-ataxic period, and no comatose period; then death. But on the seventh day 2 of these rabbits showed slight signs of ataxia and a singular state of excitation, which lasted for three to four days; after which they returned to normal and survived.

The preventive treatment with electroshocked brain had conferred upon these rabbits a special resistance to the fatal virus of rabies, in some prolonging the period of incubation, in others resulting in a complete cure following slight symptoms of encephalitis.

Upon the conclusion of these two series of experiments, one on patients and one on rabbits, I felt that I could state that following repeated electroshocks "highly vitalizing substances with defensive properties" are formed in the brain in the supreme struggle, to which I proposed to give the name *acro-agonines*, from *akros* (extreme, supreme) and *agon* (struggle, defense) (1947).[52]

Subsequently these results were largely confirmed in the clinical and the experimental fields alike, both by ourselves and our immediate collaborators and by other researchers.

In the earlier phases of our own research, we sometimes found discrepancies in the results; but as we continued testing and retesting, we became aware of certain conditions in the preparation of the acro-agonines that were capable of modifying their efficiency. Thus, for example, having started out with the oversimplified notion that maximum effects should be achieved with the maximum applications of electroshocks to pigs, we found ourselves obliged to recognize the error of this view. In this connection, we were considerably influenced by the experiments of Longhi and Martinotti and their concept of the "cumulative syndrome" that is a result of electroshock application. They demonstrated that an excessive number and frequency of applications brought about functional exhaustion in the diencephalic and mesencephalic centers (i.e., annihilation). We consequently reduced the number of electroshocks considerably (to 10 to 12), performing them on alternate days, and sacrificing the animals one or two days after the last application.*

Another important factor was the age of the preparation. As occurred in the case of the antirabic vaccine, the vitalizing and defensive properties of the aqueous suspensions of electroshocked brain diminished quite rapidly during the period concerned, so that after one and a half to two months, these properties were considerably reduced. This, as will be seen, we tried to counteract by special treatments in the course of preparation.

In other series of experiments we endeavored to associate the properties conferred on the brain substance with repeated convulsions by producing biologic stimulins in the brain in the manner of Filatov, keeping the brains under refrigeration for a number of days prior to preparing the suspensions. The results of these experiments were interesting but, by the same token, not yet definitive (D'Angelo[54]).

(a) In the experiments on patients, the actually interesting results obtained in connection with the endogenous dysthymia cases again appeared in a conspicuously clearcut manner, particularly in the manic-depressives. We were able to experiment on patients at frequent and regular intervals; for the patients, well recognizing the first symptoms of the morbid episode, took prompt recourse to acro-agonines in their various successive episodes and were returned to normal with only four or five injections (Longhi).

Not many experiments were performed on schizophrenics. On the other hand, the treatment of a serious organic disease, senile dementia, was attempted (D'Angelo, Dell[55]) with

* The rate of growth of methylcholanthrene sarcoma in mice is considerably reduced by repeated emotional stress (Rashkis[53]). This effect lasts approximately two weeks: then the sarcoma proliferates rapidly again—whether or not the stress is administrated. This would be a reasonable field of research to test electroshock power if any, perhaps with quantitative evaluation.

interesting results: the cessation of insomnia and psychomotor agitation and, in 3 cases, "an evident regression of the demential state," which, however, lasted only a few weeks.

Gley, Rondepierre, and Oules (1950)[56] prepared the brain of electroshocked rabbits "in various manners, but, in general, the method of extraction was similar to that still employed for insulin." In patients with periodic psychoses, no modification of the physical or mental state was observed when extracts of un-electroshocked brain were used; whereas with ten injections of extract of electroshocked brain, given one per day to 37 subjects, there were 10 cures resulted, 13 improvements, and 14 failures.

Alves Garcia (1950),[57] in the treatment of a hundred patients in the Rio de Janeiro Psychiatric Institute, observed "notable modifications of insomnia and dysthymia." He particularly developed the use of acro-agonines in the regularization of sleep.

Likewise, Kornmüller (1951)[58–59] treated endogenous depression patients with extracts of the brains of rabbits which had been subjected to a series of electroshock applications, prepared by means of a special extraction technic of his own and found beneficial effects on their "affectivity, initiative, and consciousness." Kornmüller, however, stressed the sedative properties of the extracts, which had a useful function in maniacal states. He, too, noticed the prompt reactions of the neurovegetative system that I had described, as well as the favorable modifications of the mental state (particularly the cessation of anxiety and psychalgia in melancholiacs) and of the physical state (increase in weight, etc.).

Dell (1952),[55] a physician from St. Anne in Paris, carried out painstaking experiments on 41 patients in the Psychiatric Hospital in Rome, with acro-agonines prepared by us, confirming the good results on patients with various types of endogenous dysthymia, and at the same time integrating the experiments of D'Angelo on senile dementia, in which he confirmed the improvement in behavior and sleep in the entire group of patients who had symptoms of agitation. A number of experiments performed on agitated schizophrenics were without encouraging results. In 2 cases of Parkinson's disease, he found a notable reduction in oculogyric crises.

(b) In the experimental field, the results of our research (published in 1947) have received numerous confirmations and undergone interesting further developments.*

We repeated on a large scale (with 50 animals) our experiment in which rabbits were subjected to preventive preparation with 25 injections of electroshocked pig brain suspension, followed by intracerebral inoculation of a fixed virus of highly virulent rabies furnished by the Istituto Superiore di Sanità, which was known to kill rabbits regularly within a period of 5 to 6 days. In practically all the rabbits, a prolongation of the incubation period of varying duration was found, as well as a prolongation of the ataxic and comatose periods, so that the animals died in accordance with a time curve which ranged from seven to thirteen days (1949–50).

---

* Injections of brain substance of shocked pigs were found beneficial in cases of ozena, both subjectively and objectively (reduction of sloughs and diminished fetor) (Mancioli[65]).

We have often seen hair loss stopped by acro-aginins, and new hair actually grow (cf clinical trials by alopecia by Tommasi[67]).

In 1950, Martinotti[60] repeated the experiment, preparing the rabbits with daily injections of electroshocked pig brain suspension and then inoculating them with the fixed virus of rabies. Out of 20 rabbits, 9 died at the same time as the controls; 7 died from one to five days later; and 3 survived.

Doctor J. M. Hirsch,[61] with four colleagues at the National Institute of Hygiene in Caracas, performed experiments on rabbits in which he treated them with preparations of electroshocked brain, after which he inoculated them intracerebrally with fixed virus. Whereas all the controls (which had been treated with normal brain) died on the sixth or seventh day, 3 of 10 of the other group survived. Out of a series of 5 rabbits, that had received preventive treatment with 15 applications of electroshock over a period of 21 days, 1 survived.

The 4 rabbits that survived were again subjected to intracerebral inoculation with the virus a month later. Of these, 1 was found dead on the sixth day, without having presented any pathologic symptoms. The others were completely unaffected.

Bonfiglio, Jr., (1948)[62] after preventive injections of electroshocked rabbit brain in rabbits with experimental toxoplasmosis (positive fluid), observed that the active onset of the disease was delayed by seven days in contrast to the control rabbits previously treated with un-electroshocked brain suspensions.

Accornero (1947)[63] observed that an epidemic of pasteurellosis in rabbits was survived by the animals which had received preventive treatment with electroshocked sheep brain, whereas those that had been treated with normal sheep brain died.

Of particular interest are the experiments of Spolverini (1948),[64] who, at the Istituto Superiore di Sanità, subjected groups of monkeys to preventive preparation with daily injections of acro-agonines and thereupon inoculated them intracerebrally with a highly virulent virus of poliomyelitis of constant lethal properties. In contrast with the controls prepared with un-electroshocked pig brain, all of which died, it was found in this first-mentioned group that the acro-agonines had conferred upon them a special resistance to the poliomyelitis, in some of the animals delaying the appearance of the characteristic syndrome of the disease, or rendering it mild and limited in effect; while in other animals it actually had the effect of preventing the appearance of any manifestation of paralysis whatsoever, though the latter did show the characteristic fever curve of poliomyelitis.

From all the tests on man and the experiments on animals, then, we find: (a) a clearcut difference between the properties of the brain of animals subjected to electroshock and those of the normal brain; and (b) that suspensions and extracts from the brain of electroshocked animals possess beyond any doubt distinctly vitalizing defensive properties in the treatment of some "endogenous" mental diseases, as well as in that of some organic diseases of the brain.

These special properties shown by the brain substance following the repeated application of electroshock are explained either as the manifestation of defensive properties normally latent in the brain, or as involving the production of new substances, or as due to both these factors.

Since it appears to us that no further hypotheses are warranted, we have designated the process *generically*, admitting, simply, the appearance in the brain of "defensive and vitalizing

substances provoked by extreme danger" (viz., acro-agonines) when the subject is exposed to electroshock.

Naturally enough, this has given rise on the part of a number of authors, to attempt a more refined interpretation of the phenomenon in question.

(A) First and foremost, the obvious question has been raised as to what part of the brain is responsible for the maximum production of the acro-agonines.

Garcia has definitely aimed at establishing a difference between the hypothalamus-diencephalon and the rest of the encephalon, and he has experimented with fractionated extracts from the two portions of the hypothalamus, the anterior and the posterior. He found that the extract of the anterior portion (preoptic and supraoptic) contains a substance which induces "a rapid state of fatigue, depression and sleep," while the extract from the posterior (retro-mammillary) portion "produces—apart from a lowering of the arterial pressure—a state of excitation and vivacity of the consciousness comparable to that produced by benzedrine, and also hinders sleep." As shown by my previous (1940) focalization of the epileptogenic constellation activated by electroshock in the meso diencephalon—and with regard to the humoral part, in the diencephalon in particular—I, too, briefly entertained the idea of restricting the field of research, with respect to the acro-agonines, to the diencephalon. But it seemed preferable to attack the problem of the acro-agonines in an integral manner, seeking these substances in the entire cerebral mass, all of which, more or less, participates in the electroshock stress. I feared that, because of the great complexity of the reactions unleashed, the involvement of other portions of the brain, which conceivably collaborate with the diencephalon might be lost, and it seemed premature to study separate parts of the brain. I did not consider the cerebellum and the spinal cord. I was also concerned with the quantity of brain substances at my disposal, which is why I rejected the brain of rabbits as too small and preferred that of pigs, which would furnish me with over 100 Gm. of brain; in addition to which, the brain of the pig is of a phylogenetic stage closer to that of man, as compared with the lissencephalic brain of the rabbit.

All in all, Garcia's research based on the distinction of the diencephalon from the rest of the brain, as well as a distinction between the two portions of the hypothalamus, standing in relation as it does to many other neurophysiologic studies on the subject (cf. Hess[68] and others), continues to be of greatest interest in the field of pure neurophysiology.

(B) Another problem that has concerned me since I first began my research on acro-agonines has been to what extent, if at all, I should use extraction methods in the preparation of the brains of electroshocked pigs, and proceeding, in other words, to the chemical fractionization of the brain substance.

Garcia, in his first experiments, made use of a "saline extract of the diencephalon, following the technic recommended by Prof. Cerletti (acro-agonines)," and "in glycerinated physiologic solution, kept at a *p*H of 6.8," he performed successive fractionization in extracts, producing precipitation by means of common agents which flocculate the globulins united with the glycides and the lipids. He suggests that the active substances belong to the protein group, while the lipids as such, which are separated by means of decantation with alcohol, ether or acetone, are, he claims, endowed with activities which are negligible from

the physiologic and therapeutic point of view, in addition to which they readily undergo alteration.

We have seen that Gley, Rondepierre, and Oules adopted "a method of extraction similar to that still used for insulin."

Kornmüller bases his procedure on the hypothesis that the active substances are liposoluble. He begins by intense extraction with acetone, thereupon eliminating the acetone to the point of exsiccation, after which he continues the extraction with Soxhlet's apparatus. He then dissolves the extract in olive oil with the aid of petroleum ether at a low temperature, subsequently eliminating it by heat in a vacuum water jet. The dry extract is 7.3 per cent the weight of the brain in rabbits, and 7.8 per cent in monkeys. He completely removes the phosphatides, which he believes do not present any activity. The extracts he used in his experiments were obtained in this manner.

It is worth noting that Kroll, in his research on sleep (1933), undertook to extract the liposoluble elements from the brains of rabbits, and that these substances, when taken from the normal brain and injected in rabbits, produced no appreciable effect; in contrast to which, when they were taken from (a) rabbits that had been put to sleep with pernocton, (b) rabbits that had been subjected to electronarcosis, and (c) the brains of hamsters and hedgehogs that had been killed after 40 days of hibernation, they produced in the injected rabbits a profound and prolonged sleep.

Inasmuch as I am completely inexpert in the arduous problems of biochemistry, and in consideration, further, of the disagreements among the authors with regard to the values of the different substances separated by various methods of extraction, I have thus far abstained from following the invitation of chemists to undertake any chemical fractionization of the brain, for fear of possibly losing thereby some of the active substances of the electroshocked brain.

I have tried only, with the help of able technicians, to exsiccate the brain substance by lyophilization—an anything but easy process—in view of the poor stability of the aqueous suspensions of the brain *in toto*; and today we finally have at our disposal a good, dry brain powder which has been shown to be satisfactorily soluble in aqueous media.

Another practical problem we have had to give serious consideration has been the sterilization of the lyophilized substance in such a way as to minimize the alterations to which it might be subject as the result of high temperatures, etc.

(C) Now that the actual existence of the acro-agonines has been established, the question has arisen in many quarters as to just what they are.

Garcia, referring to a thesis he worked out largely during the years 1949–50, attributes to the hypothalamus, in addition to its functions as a neurovegetative center, a "genuine, active internal secretion" of its own, and not merely the function of fixing the products of hypophysis (the "hormonopexia" of Remy Collin).

Kornmüller posits the existence of secretory properties on the part of special cells in the grey substance, and specifically, the "satellite" nerve cells, or "Trabantenzellen" of the Germans, which are closely allied to the nerve cells. He calls them "Hüllplasmodien." The latter, he maintains, produce substances which penetrate the adjoining nerve cell,

regulating its excitability, and functioning as veritable neurohormonal glands. The EEG, according to Kornmüller, is for the large part an expression of the activity of these glandular elements. In animals which had received injections of the extracts of the brain of rabbits which had been subjected to numerous electroshocks, he reports EEG findings which were the same as those normally obtained in postelectroshock states—a new and interesting proof that the mechanism of electroshock action consists either partly or entirely in the production of acro-agonines.

The question has also been raised as to whether the mechanism of action of the acro-agonines is analagous to the poststress effects amply illustrated by Selye,[69] or in other words, whether electroshock action has the effect of liberating ACTH. It is quite possible that electroshock, as a powerful discharge going out from the diencephalon, also stimulates the liberation of ACTH, as Selye has demonstrated; but it seems to us that the acro-agonines cannot on that account be identified with ACTH. It must be observed, in the meantime, that the latter hormone in its pure state has been shown to be ineffective in the treatment of mental diseases, and for that matter has been known to release maniacal or depressive or paranoic syndromes, effects which have never been observed with acro-agonines, of which the effects, if anything, are sedative and restorative. And finally, while, according to Selye, the hormonic response is immediately after the stress, our experiments have shown that the optimum production of acro-agonines occurs two days after the last electroshock of a series.

It will probably be possible to clear up this point by instituting parallel studies concerning the comparative use of ACTH and the acro-agonines.

Summarizing then, concerning the nature of acro-agonines and the mechanism by which they are produced, we have, thus far, nothing but hypotheses; I do not consider it appropriate for the time being to become involved in this thorny field on the basis of purely theoretical conjectures.

It is evident that the solution of these problems lies within the domain of the biochemists. For some years now I have been soliciting their aid, and a certain number of them have manifested their interest in the question. The major difficulty which stands in the way of any rapid advance in this research is the lack thus far of a rapid and convenient test. The biologic tests at our disposal are still far too slow and complicated: (1) the tests on mental patients which require a very exact clinical study over a considerable length of time; (2) the tests on animals designed to show the enhancement of their organic powers of resistance to encephalitis produced by the virus of rabies, to poliomyelitis, to pasteurellosis, to toxoplasmosis, and, undoubtedly, to other diseases as well—all tests which are both complex and lengthy; (3) Demole's[70] sleep test, already successfully applied by us (Longhi), involving the injection of a droplet of acro-agonines in the periventricular grey (III ventr.) of dogs, that produces a profound and prolonged sleep, which does not result in the controls which have received injections of normal brain—this, too, a quite delicate test; and (4) the test with the use of EEG's proposed by Kornmüller, which gives promise of practical application.

Needless to say, we are anxiously in quest of simpler and more demonstrative tests, and we are in the process of organizing the large-scale production of standardized acro-agonines to make them generally available to biochemists.

When the latter, with their methods of fractionizing the substances contained in the electroshocked brain, have isolated the active substance or substances, we shall then be able to proceed with the rational preparation of brain *extracts*, as well as to determine with the desired precision the doses best suited for application to patients and for experimental research on animals.

As can be seen, a long and demanding path lies ahead, and one along which I, for lack of competency in biochemistry, cannot proceed. But in order that we should not remain inactive, we can, I think, meanwhile, make acro-agonines better known by following a scientific path which is less well defined but which may well contribute new knowledge, and that is the path of ample clinical-statistical research. We will not yet have arrived thereby in the domain we should all like to reach of the "logical therapy" in the sense recommended by Peters;* but, by using acro-agonines in the treatment of large numbers of patients and in the most varied diseases, we shall be able to make useful contributions to a number of problems. With this in mind, as noted, steps are being taken to organize the large-scale production of acro-agonines, prepared in accordance with the empirical precepts which have emerged from the several years of experimentation thus far devoted to the matter, in order to be able to supply adequate quantities to laboratories and major hospitals.

After this tiring and sometimes thankless excursion along the rugged roads and byways of scientific research leading to the limits of human knowledge, may we be permitted a digression which will give us pause to take courage in our striving for the truth.

In the word "acro-agonines" is contained the concept of the extreme struggle for survival. The reference is to the final struggle which every organism makes when it finds itself facing the portals of death, the extreme struggle which from time immemorial has been called "agony." Now, there is an interesting and little known work by Icard[73] entitled *L'âme des mourants* that contains an abundance of suggestions on the subject of the mechanisms of extreme defense set in motion by the brain during agony. Agony is conceived as a slow asphyxiation which, according to Icard, includes excess of CO_2, a lack of oxygen, and the accumulation of toxins in the blood.

It is a question of a poisoning which, while it promotes weakness, also has excitomotor power that affects the nerve centers (Bertin).[74] According to Icard, now, the progressive slowing down of the organic exchange processes, instead of bringing about inevitably the arrest of the psychic functions, in certain cases endows them with renewed strength and produces unexpected manifestations of vitality. It is thus that Icard explains the phenomena of hypermnesia and panoramic survey of the past, so often observed in those in the agony of death; the exaltation of intelligence in the last moments of life: extasis, vatici-

---

* Peters[71] has shown that substances which inhibit the pyruvic oxidase system may induce convulsions in pigeons. In this case, as in many of the kind, it has been shown that the metabolic mechanisms that supply energy to the cells have been impaired. This is actually the main factor of the "chemical damage."

Why lack of energy should produce convulsions is still unknown.

Hastings et al[72] have shown that changes of inorganic ions content in C.S.F. lower the threshold of excitability, but no relationship has been so far demonstrated between these two groups of phenomena (disionia and biochemical damage).

natio morientium; and the recovery of reason by some of the insane when they are on the point of death.

By purely analogic association, one is led to suppose that a new articulation is to be inserted in these phenomena so frequently recorded, namely, that of the more active formation of the acro-agonines.

BIBLIOGRAPHY

1. Chiauzzi: Pathologica, 26:1934.
2. Bini: Arch. Suisses De Neurol. et Psychiatr. 39:1937.
3. Cerletti: Atti d. Convegno S. Terap. d. Schizofr. Soc. Lomb. Med. 16:1937.
4. Cerletti: Boll. e Atti della R. Accad. Med. di Roma. 63:1937.
5. Cerletti E. Bini: Boll. e Atti della R. Accad. Med. di Roma. 64:1938.
6. Cerletti E. Bini: Riv. Sperim. di Fren. 64:Fasc. II, III, IV 1940 p. 105–153.
7. Bini: Riv. Speriment. di Freniatria. 64:Fasc. II e III, IV 1940 p. 155–252.
8. Accornero: Riv. Sperim. di Freniat. 64:p. 253, 1940.
   ———————Lavoro Neuropsich. N. 3:1948.
9. De Laurenzi: Riv. Sperim. di Freniatria 64:p. 275, 1940.
10. Vattuone: Riv. Sperim. di Fren. 64:p. 283, 1940.
11. Felici: Riv. Sperim. di Freniat. 64:p. 307, 1940.
12. Castellucci: Riv. Sperim. di Freniat. 64:p. 317, 1940.
13. Bertoloni: Riv. Sperim. di Freniatr. 64:p. 325, 1940.
14. Ciotola: Riv. Sperim. di Freniatr. 64:p. 335, 1940.
15. Ferreri: Riv. Sperim. di Freniatr. 64:p. 343, 1940.
16. Flescher: Arch. Svizzero di Neurol. e Psich. 48-n. 1:1941.
17. Longhi: Riv. Sperim. di Freniatr. 64:p. 353, 1940.
18. Challiol: Riv. Sperim. di Freniatr. 64:p. 429, 1940.
19. Rizzo: Riv. Sperim. di Freniatr. 64:p. 443, 1940.
20. Bini E. Puddu: Riv. Sperim. di Freniatr. 64:p. 447, 1940.
21. Cerletti: L'Elettroshock. Riv. Sperim. di Freniatr. 64:Fasc. II, III, IV, 1940.
22. Felici: Bollet. Sanit. Tripolitania: 1944.
23. Cerletti: Congres internaz. de Psychiatrio. Paris 1950. Hermann Ed.
24. Cerletti: Congres mond. de Psych. Comptes rendus des séances. Hermann Paris p. 11:1952.
25. Bollea E. Manfredi: Lavoro Neuropsich. 1 Fasc. 3:1947.
26. Kroll: Die neuropathol. Syndrome. Berlin Springer: 1929.
27. Kuppers: Psych. en Neurolog. Bladen 4-.1938.
28. Haskorec: Revue Neurol. 33.1-1925.
29. Camus: Paris Medical 1922.
30. Hess: C.r. de la Soc. de Biologie n. 25:1931.
31. Kleist: Episod. Dammerzust Leipzig & Thieme: 1926.
32. Rohrbacher:
33. Gamper: Ed. Schlaf, Delirium Tremens—Korsakowsches syndrome Zbl. Neurol. 51, 236:1929.
34. Duret:
35. Berner, E. Neuburger:
36. Redlich, E.: Zeitsch. f. die Gesamm. Neurol. u. Psych. b. 95 s. 256.
37. Strauss:
38. Kamper:
39. Boon: Haarlem De Erven Bohn: 1938.
40. Karplus, J. P., E Kreidl, A.: Gehirn in Sympathicus I-II-III-IV-V, Pfluger's Arch. ges. Physiol. 1909—129–138, 1910—135–401, 1912—143–109, 1918—171–192, 1924—203–533.

41. Delay: Method. biolog. en clinique Psych. Paris Masson: 1950 p. 151 et suiv.
42. Longhi E Martinotti: Clin. Nuova Suppl. 1948—1 & 6.
43. Arsuini E Bondolfi: Quad—Scientif—Dello Smeraldo—Genn. 1953.
44. Merucci: Archivio De Vecchi—17:Fasc. 1, 1951.
45. Verdozzi Masini Novelli Biaggini: Boll. Soc. Gt. Biol. Sperim *25*:1949.
46. Bard, P.: Amer. J. Physiol. *84*:p. 490, 1928.
47. Cerletti: Amer. Journal of Psychiatry. *107*:2. Aug. 1950.
48. Cerletti, Longhi, Martinotti: Premier Congrés de Psych. Paris IV Comptes rendus des séances p. 224 Hermann 1952.
49. Cerletti: Allyc. Atti Soc. Lomb. Scienze med. e biol. *13*:f. 6, 1925.
50. Roos E. Koopmans: The veterinary Journal 90:1934.
51. Doussinet et Jacob: Annales Med. Psych. 5—1945.
52. Cerletti: Lavoro Neuropsich. *1*:Fasc. III, 1947—367.
53. Rashkis: Scientia London: 1950.
54. D'Angelo: Ospedale Psichiatrico Roma: 1951.
55. Dell: Resoconto scritto Osp. Psich. Roma: 1952
56. Gley Rondepierre Oules: Congres Intern. de Psych.: 1950 Paris Hermann.
57. Garcia: Regolazione ormobale del sonno: 1950.
58. Kornmuller: Zschr. d. Neurol. u. Psych. *19*:Fasc. 8, 1950.
59. Kornmuller: Zschr. d. Neurol. u. Psych. *19*:Fasc. 12, 1951.
60. Martinotti: Lav. Neuropsich. *2*:Fasc., 1950.
61. Hirsch: Relaz. dattil. *2*:Apr. 1952.
62. Bonfiglio, Jun.: Osp. Psych. Roma: 1948.
63. Accornero: Lav. Neuropsich. *2*:Fasc. II. 1947.
64. Spolverini: Acta Paediatrica Latina *2*:1949.
65. Mancioli: Atti del *37*: Congress d. Societa di Otorinolaringoiatina: 1948.
66. Menichella: Sanare. Anno II. Fasc. 3. Nov., Dec., 1950.
67. Tommasi: Ann. di Dermatol. e. Sifil. 2–518, 1949.
———: Atti d. Societa di Dermat. e. Sifil. 28–30 Mag., 1948.
68. Hess: Das, Zwischenhirn. Benno Schwabe Basel: 1949.
69. H. Selye: The general adaptation syndrome and the diseases of adaptation. J. Clin. Endocrin. *6*:117, 1946.
———: Textbook of Endocrinology. Acta Inc. (Pubs), Montreal, 1949.
70. Demole: Arch. f. exper. Path. u. Pharmakol. 1927.
71. Peters: Brit. Med. Bull. *9*:117, 1953.
72. Hasting: American Journal Physiol. *121*:179, 1938.
73. Icard: L'ame des mourants. Bibl. Eudiague. Paris: 1929.
74. Bertin: (v. Icard).
75. Delay et Soulairac: Boll. Soc. Gt. Biol. Sperim. *25*:1949.
76. Delay, Soulairac, Rurere Corteel: Ann. d'endoinnologie *5*:92, 1944.
77. Cerletti: Riv. Sperim. di Freniatria *38*:1912.
78. Longhi E Martinotti: Clinica Nuova I, 4, 5, 6, 1948.

The Convulsive Treatment

A REAPPRAISAL

*L. J. Meduna, M.D.**

CHICAGO, ILL.

Instead of the better known name, "Metrazol Shock Therapy," I have, advisedly, chosen for my title "The Convulsive Treatment." I have done so because I consider myself to have been the originator not of the metrazol, nor of the camphor, therapy alone—I have never considered myself the originator of either of these therapies—but of the convulsive treatment. It has been said that I conceded that I wanted to substitute metrazol for insulin treatment: nowhere have I made this concession for I believe that both insulin and convulsive treatment have their own indications and merits. Camphor and metrazol, and many other drugs, are only suitable means of provoking convulsions in schizophrenic patients in order to produce remissions. I had, however, worked painstakingly for many years before I reached that phase of my researches in which I could think of means of curing schizophrenia.

In order to enable the American reader to understand the uncertainty, almost the anxiety, which I harbored at the time when I first dared to think of curing schizophrenia, I must take him back to the beginning of the years which I spent studying at the Interacademic Brain Research Institute in Budapest, under my great teacher, Karl Schaffer.

Professor Schaffer was a psychiatrist *sui generis*. He began his career as a neuroanatomist; in the early phase of his work, he became a neuropathologist; and toward the end of his life, a psychiatrist. For him nothing existed in the mind if it did not exist in the tissue of the brain. As an authority on the histopathology of the heredo-degenerative diseases of the nervous system, he developed a theory of his own regarding schizophrenia. For him schizophrenia was an endogenous hereditary disease that attacked certain systems in the brain (whence his term, "systemic selectivity"), but in only the cerebrum (whence his term, "segmental selectivity"), where it afflicted exclusively the nerve cells (whence his term, "ectodermal selectivity"). Since he conceived schizophrenia to be an endogenous hereditary disease, he held that it could not be cured. As the ectoderm of the embryo was already sick and as the disease was transferred by the chromosomes, any idea that this disease could be cured was to him nonsensical. It has been said that Professor Schaffer publicly supported insulin shock therapy. Professor Schaffer never published any article on insulin shock therapy. It has also been said that Doctors Stief and Tokay, who found that insulin coma produced vasoconstriction in dogs but in no other experimental animals, worked under Professor Schaffer on the staff of our hospital. This is not so since Doctors Stief and Tokay were never connected in any way with Professor Schaffer nor did they serve on the staff of the hospital with which Professor Schaffer and I were connected.

In his belief that any endogenous disease was incurable, Schaffer was not alone. Even Bumke, who admitted that dementia praecox may not be a disease entity, stated: "At any

* Professor of Psychiatry, University of Illinois College of Medicine.

rate, it is probable that a group of these patients suffer from heredo-degenerative disease. For this group of patients any possibility of influencing the disease is naturally an *a priori* impossibility."

In order to explain the occasional spontaneous recovery of schizophrenic patients, we psychiatrists first excluded the word "recovery" from the vocabulary of schizophrenia and substituted for it the word "remission." Our doing so left us with a nice leeway for our own definition; if the patient went through a spontaneous "remission," instead of a spontaneous "recovery," we still could maintain the orthodox fiction of heredo-degeneration.

But, regardless of whether we referred to the recovery as such or as "remission," the fact of this recovery had to be explained. Therefore, we assumed that the symptoms characteristic of schizophrenia might be produced by (1) endogenous factors or (2) exogenous factors or (3) a mixture of endogenous and exogenous factors. We talked of endogenous schizophrenia as a genotypic schizophrenia and of exogenous schizophrenia as a paratypic schizophrenia. And, finally, we recognized a schizophrenia in which both endogenous and exogenous factors were discernible.

Notwithstanding our heuristic considerations, we could think of no treatment for these conditions, since we assumed that the paratypic schizophrenia would admit spontaneous remissions; and we could not treat the genotypic schizophrenia, the cause of which we thought to be somehow in the germ plasm, especially in the ectodermal germ layer.

Our therapeutic investigations, therefore, were directed toward the diseases that in psychiatry we considered exogenous. Among these diseases, the one that evoked my deepest interest was epilepsy. The beautiful slides that we could make of epileptic brains always fascinated me, and I accepted Schaffer's explanations of the great abundance of glia hyperplasia in these brains. Schaffer assumed that in epilepsy both the neuronal and the glia systems were sick; and that, consequently, not only did the glia cells multiply to substitute for the destroyed nerve cells, but, because of their affliction, they began an autochthon proliferation that linked epilepsy, through the disease of sclerosis tuberosa, to the real gliomas. Working upon biopsy material of the primary convulsant foci in several cases of so-called genuine epilepsy, I observed the extreme hyperplasia of the glia system in epileptic brains, in contrast with the apparent torpor of the glia system in schizophrenic brains. To explain the difference between the behavior of the glia cells of brains in epilepsy and the behavior of these cells in schizophrenia, I developed the hypothesis that the noxa causing epilepsy has a stimulating effect upon the growth of the glia cells, while the noxa producing schizophrenia has an opposite, a paralyzing, effect on the glia system. Thus, fairly early, I developed an idea of some sort of antagonism between the behavior of the glia system in epilepsy and the behavior of this system in schizophrenia.

Later, in about 1930, I became acquainted with Dr. Julius Nyirö, who told me that, in 1929, he had been interested in epilepsy and in its combination with schizophrenia, and that he had found that schizophrenic processes have a benign effect upon the epileptic process. In 1929, in collaboration with Jablonszky, he had published, in the *Hungarian Medical Journal*, a report of his work, in which report he had thus given his final conclusions: "We found during our investigations that in those cases of schizophrenia which later became

combined with epilepsy, the epileptic attacks either had disappeared completely or had occurred only very infrequently. In cases of those who for many years had suffered from epilepsy and had later developed a schizophrenic disease, the epileptic attacks had at the beginning of the schizophrenic disease become less frequent and had later disappeared completely." In one patient who had suffered from epilepsy for many years, Dr. Nyirö had noted that a schizophrenic disease had developed, that then the epileptic attacks had completely disappeared, and that a year later the patient had had neither schizophrenia nor epilepsy but had completely recovered. After examining 176 cases of epilepsy, Nyirö and Jablonszki had found that of the uncomplicated cases of epilepsy, 1.05 per cent had recovered, while of the epilepsy cases which had been complicated with schizophrenia, the epilepsy had disappeared in 16.05 per cent. On the basis of his observations, Nyirö had assumed that the schizophrenic process must have a curative effect on the epilepsy and had begun his investigations of this probability by transfusing schizophrenic blood into epileptic patients. It is of historical interest that after several schizophrenic blood transfusions one of his first 10 cases of epilepsy was cured. Because of the prevalent concept of endogenous degeneration, Nyirö did not even think of treating, conversely, schizophrenic patients by transfusing into them epileptic blood or by provoking in them epileptic attacks.

My conclusions from Nyirö's observations were the reverse of his. The epileptic process, I assumed, might have, probably through its stimulating effect upon the torpid glia system in schizophrenia, a beneficial effect upon the process of schizophrenia itself. I assumed, therefore, that there must be some sort of antagonism between epilepsy and schizophrenia. My assumption was confirmed by a finding of G. Steiner and A. Strausz. These authors had found, among more than 6,000 patients with schizophrenia whom they had examined, only about 20 in whom epileptic attacks had occurred; and they had ascertained that even these very rare attacks had mitigated the schizophrenic process. Their final conclusion had been that typical epileptic attacks, if they occur at all in true schizophrenia, are so rare that the correctness of the diagnosis of schizophrenia should at first be doubted.

The observation that gave me the final decision to work on the convulsive treatment was one published by G. Mueller in 1930.* Mueller had reported upon two catatonic patients who had developed spontaneous epileptic attacks, after which the patients had recovered from both the epileptic and the schizophrenic forms of disease. The connection between the appearance of the epileptiform attacks and the disappearance of the schizophrenia had been so striking that at the end of his article Mueller had remarked: "The beneficial effect of the epileptic attack upon the schizophrenic process reminds me of the beneficial effect of high temperature upon the course of general paresis."

From that time on, I was convinced that there is a biological antagonism between the process which produces epileptiform attacks and the process which produces schizophrenia. I had only to find a convulsant drug which could be used safely in human beings, which would produce epileptic attacks by acting upon the nerve cells of the brain, and which would leave the cerebral blood vessels intact.

---

* Allg. z. Psych., 83.

At that time (1933), we knew of many drugs that produced toxic epilepsy, such drugs as picrotoxin, absinthe, antipyrine, and camphor. We knew that camphor produced epileptic attacks that stimulated the cortex of the brain; but I could not find any data upon the toxicity of camphor. I did not know the lethal dose of camphor, and I could not find in the literature any data about whether camphor would attack and injure the blood vessels of the brain. The behavior of the blood vessels was of great importance. At that time, the German school of histopathology—Spielmeyer, Spatz, and others—maintained that in epilepsy the pathologic changes in the nerve cells and the consecutive changes in the glia cells were caused by spasm of the blood vessels in the brain during attacks; while we in Hungary maintained that the spasm of blood vessels had no genetic role in the epileptic form of attack.

My experiments, which were to lead to my origination of the convulsive treatment, I began in November, 1933, by trying to produce chronic and acute camphor poisoning in guinea pigs. I found that the camphor sensitivity in these experimental animals varied greatly. I had some guinea pigs which developed epileptic status and died from 2 cc. of oil that contained 25 per cent of camphor, while some others tolerated up to 10 cc. of camphorated oil, that is to say, 4 to 5 Gm. per Kg. of body weight.

This finding gave me a clue about the beginning dosage of camphor, which I should later use in my human experiments. I examined the central nervous systems of my guinea pigs by using the staining methods (1) of Nissl, (2) of the Sudan stain for fat, (3) of Van Gieson, (4) of Spielmeyer, and (5) of silver impregnation, according to Hortega. My experiments with camphor poisoning in guinea pigs led to my making these five observations:

1. Camphor poisoning in guinea pigs produces epileptiform attacks that show the greatest possible analogy with attacks in human epilepsy.

2. The blood vessel system of the animals that die in epileptic status produced by camphor poisoning is perfectly normal.

3. The pathologic changes in the nerve cells in the camphor-treated guinea pigs are diffuse and independent of the blood vessels.

4. The pathologic changes present a typical case of ectodermotropic poisoning.

5. The greatest degree of pathologic change in the nerve cells occurs in the medulla oblongata—a phenomenon which I consider to be an example of Vogt's pothoklysis.*

By the time (1934) of my publication of these observations relative to camphor poisoning in guinea pigs, my experiments in using camphor to produce epileptiform attacks in human beings were already in process. The results of my first observation in connection with these human experiments I published in January, 1935† under the significant title, "Attempts to

* Arch. z. Psych., June, 1934, p. 102.

† As a matter of record, I gave the first camphor injection to provoke epileptic attack in a patient on January 23, 1934. I published my observations on the first 26 cases given convulsive treatment on January 18, 1935. Many times have my friends asked me why I delayed my publication for a whole year. The answer is simple: Karl Schaffer, the old master, whose pupil I was, was a scientist of the most rigorous integrity; and he would have opposed the publication of observations upon fewer than 25 cases. Had I published observations which I had made upon only five or even 10 cases, he would forthwith have cast me out as his student—as he once sternly told me that he would do if I became concerned with utilizing the metrazol treatment for the making of money. (As a matter of fact, never in my life have I accepted a medical fee for metrazol treatment.)

Influence the Course of Schizophrenia by Biological Means." This title I call significant because it shows that, at that time, I was not altogether convinced that the epileptiform attacks that I had produced in these patients had been the factors responsible for the change in the course of their disease.

In this paper I reported that in 10 of the 26 patients the disease had changed so favorably that I had felt it necessary to analyze the histories of these 10. After a survey, I had found that neither in the heredity nor in the clinical picture of these patients was there discernible anything that differentiated them from the 16 other patients whose condition had not been changed at all by the injections of camphor. Therefore, I had felt that I was dealing with two different groups of patients: one group in which the schizophrenic process had been changed by the camphor injections, and another group in which the course of the disease had been unchanged. In looking for the factor that would differentiate these two groups, I had found that this factor was either the camphor tolerance or, specifically, the epileptic diathesis of the patient. Comparing 10 patients of one group with 10 of the other group, I had reached the following conclusions:

"The total weight of 10 patients whose schizophrenic condition was unchanged was 558 kilograms. The number of injections in this group was 128; the amount of camphor injected, 700 grams; the number of epileptiform attacks, 62.

"The total weight of the 10 unchanged patients was 589 kilograms; the number of injections, 229; the amount of camphor, 1,293 grams; the number of epileptic attacks, 25.

"Thus, in the improved group, with an average of 55 kilograms of body weight, 70 grams of camphor produced 6.2 epileptiform attacks in the average patient; while in the unchanged group, in a patient with an average body weight of 58.9 kilograms, 129 grams of camphor produced only two epileptiform attacks. So the convulsive diathesis or the camphor tolerance may be the factor that separates the two groups of schizophrenic patients."

I was not convinced, *at this time*, that the remissions of the 10 cases had been caused by the epileptic attacks that I had produced, for another explanation was possible: a group of schizophrenic patients is characterized both by a tendency to remissions and by convulsive diathesis. If the two phenomena (i.e., tendency to remissions and the convulsive diathesis) are correlated factors, the diathesis in schizophrenia would be a simple index to the tendency to remissions.

"The tendency to remission and the convulsive diathesis are in causal relation to each other or are correlated. If the convulsive attacks cause the remission, a new art, with the possibility of curing schizophrenia, is open to us. If convulsive diathesis and tendency to remission are correlated, I have succeeded in proving what I had assumed, a peculiar biological antagonism between epilepsy and schizophrenia."

From this quotation it is easy to see that at that time—during 1934 and up to the publication of my report in January, 1935—I was not altogether sure whether I had really found a new therapeutic method. The question whether the camphor procedure could be considered a new therapeutic method, or whether it had uncovered a correlation between a tendency to spontaneous remissions and convulsive diathesis, I could answer only by statistical method. Such an answer I now attempted to secure.

By trying to work on a greater number of patients, I found the camphor method, for technical reasons, less and less useful. The great amount of camphor necessary to be injected made the technique cumbersome; moreover, we had to wait several hours before one attack, and frequently several attacks, of epilepsy would occur. These inconveniences in the use of camphor made me look for a better convulsant drug; and, in 1934, I began to use cardiazol, a drug known in the United States as metrazol. Because of the facility of intravenous administration of metrazol, the convulsive treatment with this drug became much easier and was therefore tried with more willingness by many authors than would have been this treatment with camphor.

In 1935, I was already able to report upon 101 patients to whom I had given the convulsive treatment; I did so in "The Convulsive Treatment of Schizophrenia."* The title of this paper shows that at the time of the publication I was already convinced that I had originated a new treatment for schizophrenia. In this paper I emphasized that the shorter the duration of the disease, the greater are the chances of the patient to benefit from this treatment. In this paper I stated that if the process phase of the disease has terminated, the patient's chances to benefit from this treatment will greatly decrease. In this paper, furthermore, I made the statement, at that time revolutionary, that "the selection of the patients for this treatment should be made regardless of the symptoms of schizophrenia and *regardless of the hereditary taint* present." In this paper, on the basis of my statistical material, I reported the fact that the probability for remission in any particular case is greater if the patient reacts with a stronger epileptic attack to a comparatively small dosage of metrazol—in other words, that the probability of remission is in direct relation with the convulsive diathesis of the patient. Out of 101 cases that I had treated before the publication of this paper (in 1935), I had obtained 41 total remissions.

Previously to the publication of the paper to which I have been alluding, I had written, in English, a short report entitled "New Methods of Medical Treatment of Schizophrenia." For reasons unknown to me, however, this report was published (in the *Archives of Neurology and Psychiatry*)—only in 1936. In this earlier paper I had mentioned both the camphor and the metrazol treatments. I had been in doubt, however, about the comparative value of the two drugs, wherefore I had written: "The convulsions caused by the two substances (camphor and metrazol) are similar. As yet, however, I am in no position to judge that the remissions caused by these substances are of equal value." In this paper I reported that of 43 patients whom I had treated, 19 had been cured, seven had shown improvement, and the condition of 17 had remained unchanged. I had reported, also, that Dr. A. Z. Rath, the first re-investigator of my claims, in his experiments had used camphor only; and that of his 31 patients, 10 had been cured, 4 had shown improvement, and the condition of 17 had remained unchanged. In my conclusion I had written: "For a full evaluation of the number of cures, it is necessary to emphasize that the material consisted mostly of patients with a chronic condition, chiefly of 2 to 3 years' duration. I am convinced that experiments carried out in a larger number of patients who had been sick no longer than six months,

* Psychiat.-neurol. Wchnschr. 37:317–319, 1935.

would lead to considerably better results. These results do not affect the theory of the endogenous nature of schizophrenia. The number of cures (39 per cent) is rendered even more impressive when it is remembered that the condition in 20 or 25 per cent of the 74 patients first treated is considered to be completely of hereditary nature, in which case the possibility of cure is out of the question."

Still with doubts, I concluded my report with the following remarks: "The manner in which the convulsions may lead to therapeutical effects may be explained in different ways: first, I thought of the known detoxicating effect of camphor. This possibility, however, is excluded by the similar results achieved by the chemically entirely different metrazol. Second, the shock effect of the convulsion may serve as an explanation. Easy as it may be to conceive that a catatonic stupor may be ended by a sudden shock, it is not plausible to imagine a cure for a delusion or an hallucination in this way.

"The only possibility left to explain the effect of the epileptic convulsions is that they change the chemical constituents in the organism in a way suitable for the cure of schizophrenia. Similar remissions of schizophrenia, e.g., remissions preceding death, are explainable by a pre-agonal change in the chemical milieu of the organism at the beginning of dissolution.

"Far from considering the convulsion therapy as the only possible way of curing schizophrenia, I think that it is only a first step on the as yet unaccustomed biological road of influencing the schizophrenic process. It is necessary to try other substances, as well as to search for the factor mobilized by the convulsion and causing its beneficial effect. In this way it will perhaps become possible to eliminate the convulsion and apply only its secondary effects."

This expectation of the possibility of eliminating the convulsion and applying only its secondary curative effects remains, I regret to state, but a pious desire even 20 years after the origination of the convulsive treatment.

From 1936, I became more and more interested in the ways in which and the means by which the convulsive treatment works rather than in the practical application of the treatment itself. Unfortunately, some research workers and some practitioners tried to set up some sort of competition between the insulin coma treatment—a treatment already accepted—and the newer convulsive treatment. So aggressive were they that Dr. M. Mueller, in 1937, was forced to raise his voice against that unscientific practice: "It is senseless (as has in some cases already happened) to consider the insulin and the metrazol shock treatments as competitive, opposing one against the other. Contrariwise, we have here two different therapeutic methods which, in the future, probably will supplement each other."*

With these words of Dr. Mueller, I introduced my lecture at the Congress of Psychiatry in Munsingen, Switzerland, in 1937. In this lecture, I again called the attention of the audience to the peculiar hyperplasia of the glia system in epilepsy, in contrast with the condition, one almost of paresis, of the glia system in schizophrenia; and I expressed the belief that antagonistic humoral processes are responsible for the differences in the pathologic

* M. Mueller: Fortschr. d. Neurol., Psychiat. 1937, 165.

picture. In the same report to the Congress, I reported upon the first 10 patients whom I had treated by the "cross" method. By this name I designated the procedure which I recommended for treating patients in whom either the insulin treatment or the metrazol treatment had not produced sufficient remission. In treating these patients, the therapist, I said, should cross from one method to the other. The results produced by these cross treatments indicated to me, at that time, that the metrazol and the insulin treatments had different underlying mechanisms and, furthermore, that we might be dealing with two different forms of schizophrenia, forms in which the pathologic mechanisms are different.

In closing this report, I again emphasized that schizophrenia is not a biological catastrophe; that is it caused neither by a sudden strike of the endocrine system nor by a sudden block of the mesenchyme; that it originates as a consequence of a logical chain of chemical processes that are composed of several conditional reactions; that when these pathologic reactions have reached a definite point or a definite intensity, the patient becomes schizophrenic; that both insulin and metrazol treatments break violently into the pathologic process in order to break up this process; that from biochemical examination of the "cross" cases, I hoped that, in the future, instead of breaking up violently the pathologic process by means of the shock treatments, we should be able to omit the coma in the insulin treatment and the convulsive attacks in the metrazol treatment and apply only those slow chemical processes that are produced by the explosive actions of both treatments and that are responsible for the recovery. From a report by Professor F. Georgi, I was glad to learn, at this same meeting, that research directed towards this objective had already been begun.

Professor Georgi, aided by a grant of the Rockefeller Foundation, had begun research in the biochemistry of the shock treatments. In the course of hypoglycemic coma, he had noticed that the blood sugar had begun to drop at the beginning of the insulin treatment, as had the lactic acid and the fat content of the blood; that during the same time there had been noticeable in the blood an alkaline shift; that from 60 to 90 minutes after the injection of the insulin, there had occurred a sudden reversal of this process—that the blood sugar, the lactic acid, and the fat contents of the blood had risen, and an acid shift had appeared. These compensatory phenomena, Dr. Georgi had deduced, had occurred because of the suddenly increased functioning of the adrenal glands, for at the time of the occurrence of these biochemical changes, the patients' adrenal glands had evinced an increase in blood pressure and in pulse rate. In another series of observations, he had found that 10 to 15 minutes after the metrazol epileptic attack the same changes had occurred in the blood that had occurred at about the 90 minute period during the insulin treatment.

All these observations had led Dr. Georgi to believe that a useful combination of the metrazol and the insulin treatments could be worked out; furthermore, that the most favorable time to produce the metrazol convulsions during the hypoglycemic coma must be the time when the function of the adrenal glands had begun to change, that is, about one and one-half hours after the injection of insulin. Thus had been born the second combination of the metrazol and the insulin treatments. To differentiate his method from the "cross" method, which I have described, Georgi had named it the "summation" method. He hoped that by administering this combination of treatments to patients, the beneficial effects of both

the insulin and the metrazol treatments would summate. I fully subscribe to Georgi's combination, and many times I have recommended its use to my fellow psychiatrists.

A third method of combining the metrazol and the insulin treatments had been worked out, and was recommended at the Munsingen meeting, by Dr. A. von Braunmuehl, who called his the "alternation" method. In this method, von Braunmuehl proceeded with the insulin treatment in the usual way but interrupted this treatment, sometimes for two or three days a week, within which interim he gave the patient metrazol injections to produce convulsions.

Thus in the history of shock treatments, the Munsingen meeting was a milestone because of its emphasis upon the fact that the insulin and the metrazol treatments should supplement rather than compete with each other—and because its description and recommendation of each of three methods whereby these therapies could profitably be used in combination: my "cross" method, Georgi's "summation" method, and von Braunmuehl's "alternation" method.

In still another respect was the Munsingen meeting a milestone in the history of shock treatments. At this meeting, de Bini first reported that he and Cerletti had been able to construct an electric apparatus which had produced convulsions in dogs and in hogs without having produced any brain pathology. I do not recall whether he announced to the audience that they were intending to use the electric convulsion as treatment for human patients. In private conversation, however, he and I discussed extensively the possibility of his using it with them. I encouraged him to do so, inasmuch as, from my own experiments, I finally had concluded that neither the camphor nor the metrazol, but the epileptiform attacks produced by these drugs, had been responsible for the improvements in my schizophrenic patients. Consequently, on the basis of my theory that the means of producing epileptiform attacks was irrelevant, I agreed with him that if epileptiform attacks could be produced in human beings by electricity, the results must be favorable.* As is known to every psychiatrist, this assumption proved to be correct. It was, I believe, in November, or December, of 1937, that Cerletti and de Bini first produced epileptiform attacks in human subjects by using electricity. It was then that the electric shock treatment was born.

In 1936 and 1937, reports of two other applications of the metrazol convulsions were published. The first of these reports, one by Dr. A. Schoehnmehl of Germany, was upon the use of metrazol as a means of differential diagnosis in doubtful cases of epilepsy. Doctor Schoehnmehl had assumed that the threshold dose of the epileptogenic metrazol must be definitely lower in epileptic patients than in schizophrenic patients. And Schoehnmehl had concluded that if the epileptic threshold in any patient is lower than 0.3 grains of metrazol, that patient must suffer from epilepsy. Schoehnmehl, in fact, had deduced these conclusions from 2 or 3 patients in whom the diagnosis of epilepsy had been doubtful and in whom he had been able to produce epileptic attacks with such a small dose of metrazol that neither

* I want it to be definitely understood, however, that the idea of using electrical convulsions in the treatment of mental diseases was originally formulated by de Bini and Cerletti and that my part in this matter was only one of enthusiastic approval.

in normal subjects nor in schizophrenic patients could he have produced epileptiform response. Schoehnmehl was the first to report that he had been able to break up epileptic fugues in each of 9 patients by a single metrazol attack and by the same means had been able to break up a long-lasting epileptic confusional state.

The second of these 1936 and 1937 publications of reports of applications of the metrazol convulsions was one by Professor A. Langelueddeke, who had observed that metrazol in epileptic patients produces epileptic attack that is a replica of the patient's own form of epileptic attacks. This observation was utilized many years later by Dr. Earl Walker for determining cerebral localization of brain injuries (tumors, etc.).

In 1937, on the basis of Schoehnmehl's conclusion that if the epileptic threshold in any patient is lower than 0.3 Gm. of metrazol, that patient must have epilepsy, I carried out experiments in order to establish, if possible, useful standards for differential diagnostic purposes. My experiments were carried out on epileptic patients who, for a whole week before the metrazol injection, had received, daily, 3 Gm. of sodium bromide and 0.10 Gm. of luminal (a trade name for phenobarbital). As controls, I used 15 schizophrenic patients and 5 patients suffering from general paresis. The control patients I put on the same medication as the epileptic cases. Of the 9 patients with epilepsy, one developed convulsion after the intravenous injection of 0.20 Gm. of metrazol; 6 responded with epileptic attack to 0.25 Gm. of metrazol; 1, to 0.35 Gm. of metrazol; and 1, to 0.45 Gm. of metrazol. The average convulsant dose in patients with epilepsy was 0.28 Gm. of metrazol. The controlled patients each responded with an epileptic attack to a dose of metrazol of from 0.55 to 0.90 Gm. The average epileptogenic dose of metrazol in my control group was 0.73 Gm., a dose about three times as high as the epileptogenic dose in patients with epilepsy. Inasmuch as the highest epileptogenic dose in a patient with epilepsy had been 0.45 Gm. of metrazol and the lowest epileptogenic dose in the control group had been 0.55 Gm., I chose as the dividing line between epilepsy and other disease a 0.50 Gm. dose of metrazol. If a patient, after having received the medication that I have described—i.e., the metrazol injection preceded by daily dosages, for a week, of sodium bromide and luminal—responded with an epileptic attack to less than 0.45 Gm. of metrazol, this fact I evaluated for the diagnosis of epilepsy. If, on the other hand, the patient responded with an epileptic attack to less than 0.55 Gm. of metrazol, this fact, in doubtful cases, I evaluated against the diagnosis of epilepsy. This little piece of research I reported in the following year (1938) in a lecture that I gave in Amsterdam at the invitation of the Nederlandsche Vereeniging voor Psychiatrie en Neurologie.

This particular information with respect to the convulsant dose of metrazol in epileptics is today probably obsolete and therefore useless. The science of electroencephalography, so tremendously developed since 1938, produces more reliable information about the function of the brain than is revealed by the convulsive threshold of the brain as determined by metrazol injections. But the metrazol attack, as a means of localizing a convulsive focus, is still a useful tool in brain surgery.

In the years 1935 to 1939 were published a few articles that are of great interest to medical history. The first of these publications, one by Dr. A. Glesinger, appeared in the *Wiener*

medizinische Wochenschrift in 1935. In this article, Dr. Glesinger called attention to the fact that L. von Auenbrugger, the discoverer of auscultatory percussion of the chest, had apparently used camphor in treating mental diseases. The dosage of camphor used by Auenbrugger had been decidedly epileptogenic, and many of his patients had developed epileptiform attacks. Auenbrugger had reported upon 10 patients who had suffered from a disease called, at that time, "mania virorum" and whom Auenbrugger had treated by oral medication of camphor. These patients had taken every two hours, day and night, the following :

Camphorae cum mucilagine Gummi Arabici
Drach. II. Leg. art. suactae
Syr. Diacod.
Aqu. Still. Flor. sambuc.
Misce.

According to Auenbrugger, 8 of his patients had recovered, 1 had recovered and relapsed and again recovered, and 1 had died in what today appears to have been an epileptic status.

In 1938 Dr. T. Havas published, in the *Budapest Medical Journal*, an article upon the use of camphor, in which article he called attention to a work of Dr. M. A. Weickhardt of Fulda, Germany. It seems that in 1798, in Vienna, Dr. Weickhardt had written a book entitled *Practical Medical Hand Book*. In this work, Weickhardt had recommended the use of epileptogenic doses of camphor for treatment of "Wahnsinn," a mental disease which may have been what is known today as a delusional state. Dr. Havas, in his article, also referred to a Dr. Simon, from whom Weickhardt apparently had learned of the use of camphor in mental diseases. Unfortunately, I was not able to trace down Dr. Simon's work upon the use of camphor in mental diseases.

In the same year, 1938, a person whom I did not know sent me a manuscript that had been written, in 1851, by a Dr. Szekeres. This Dr. Szekeres, who apparently was both a physician and a priest, had been sentenced to prison for his revolutionary activities against the Hapsburgs. In prison, in order to dispel his boredom, he had begun to write, in the manuscript later sent to me, his memoirs. After having described "Wahnsinn" and having discussed the treatment of this mental disease, he had written as follows: "Pauliczky recommends camphor, beginning with a dose of 10 grains, and increasing the dosage by 5 grains daily, up to 60 grains a day; then, the patient will develop dizziness and epileptic attacks. When the patient awakens from the epileptic attacks his reasoning will return."

Unfortunately, I was also unable to trace the mysterious Dr. Pauliczky. But Dr. Szekeres mentions at the end of his manuscript, 13 references, only one of which is concerned with nervous and mental disease: a work, by a Dr. Laroze of Paris, entitled "No More Nervous Disease! A Radical Cure of These Diseases by a Simple and Not Dangerous Medicine." In this work of Laroze, the French physician, Dr. Pauliczky, I believe, is probably mentioned. These data I published in an article entitled "The Convulsive Therapy of Schizophrenia—Its Past and Its Future."*

* Psychiat.-neurol. Wchnschr., 1939.

In 1937 and 1938, the authors using the comparatively new metrazol treatment began to work out proper indications for it. Doctor I. Von Angyal, I believe, was the first who recommended the metrazol treatment as the method of first choice for the breaking of schizophrenic stupor. Sorger and Hoffman of Austria, on the basis of their treatment of 100 cases, arrived at the following conclusions:

1. The metrazol treatment produces remissions amounting to
   a. 100 per cent in acute and subacute amentiform conditions;
   b. 81 per cent in acute and subacute stupor;
   c. 71 per cent in acute and subacute hebephrenia;
   d. 68 per cent in acute and subacute paranoid-hallucinatory conditions.
2. In no cases of catatonic excitement does the metrazol treatment produce a full remission.

These and similar indications by literally hundreds of authors have resulted in the following trend of today: amentiform conditions, stupor conditions, and catatonic conditions are predominantly given convulsive treatment; while cases of paranoid, hebephrenic, and simple schizophrenia are predominantly given insulin treatment or a combination of insulin and convulsive treatments.

A Belgian author, Dr. P. Verstraeten, was, I believe, the first who applied the metrazol treatment to conditions which we call melancholy and to the depressive phase of the manic depressive disease. In 1937, he published (in *Ann. Med. Psych.*) a report of his first 20 patients, 5 of whom had been "melancholia delirante"; 12, "melancholia anxieuse"; and 3, "melancholia stuporeuse." Of the 5 patients with "melancholia delirante", Dr. Verstraeten had cured 4. Of the 12 patients with "melancholia anxieuse," he had achieved 8 full remissions, 1 partial remission, and 1 intermittent remission, and had had 2 unimproved. All 3 patients with "melancholia stuporeuse" he had completely cured.

I myself, in 1937, had 1 patient whose illness I had diagnosed as presenile depression. This patient I treated for a year and a half by using successively opium, parenteral milk injections, intramuscular injections of the patient's own blood, hormone injections, and photodyne combined with ultraviolet irradiation. None of these treatments was of any avail. Finally, in desperation, I tried the metrazol treatment; and, by provoking five epileptiform attacks, I succeeded in curing this patient.

The progress in the development of the convulsive treatment that I have just traced I reported, in 1938, at the Meeting of the Nederlandsche Vereeniging voor Psychiatrie en Neurologie, in Amsterdam. About the same time, having worked up, in collaboration with Dr. E. Friedmann, of Ossining, New York, the European and the United States statistics of the patients who had been treated with metrazol, I reported at the Amsterdam Meeting concerning 590 patients with acute schizophrenia in Europe who had been treated with metrazol. In this group, the authors had achieved 53.5 per cent full remissions. And, although by that time 1,716 patients in Europe, whose illness was of one month's to 10 years' duration, had been treated with metrazol, there had been in this group 30.2 per cent of full remissions. Our American statistics covered, altogether, 1,465 patients who had been treated with metrazol. Of these 1,465 patients, 210 had had acute disease. In treating these 210, the American authors had secured full remissions in 60 per cent of the patients,

improvement in 20 per cent, and no improvement in 20 per cent. Of the 1,465 patients, 201 had had subacute disease. In treating these, the American authors had cured 35 per cent and improved 22 per cent. Of the 1,465 patients, 1,054 had had chronic disease. Of these 1,054, through treatment with metrazol 9 per cent had recovered completely and 45 per cent had improved.

Because of its great practical importance, one more application of the metrazol convulsion is worthy of mention: the use of metrazol convulsions to measure anticonvulsive activity of different drugs. By means of metrazol convulsions, pharmacologists are able to measure the degree of anticonvulsive potency of any new antiepileptic drug by using it in animals before it is tried in human patients.

The rest of the history, to date, of the metrazol treatment is well-known to everyone who has been reading psychiatric, neurophysiological, pharmacological, and psychological literature in the past 15 years. A tremendous interest in the new convulsive treatments has arisen in thousands of research men, who have used the new method in treating human patients and in investigating biochemical and physiologic features in animal experiments. The literature relative to this development I have been able to follow only up to 1940; but by that time I had collected abstracts of 3,900 scientific papers published in Europe and in the United States. Since 1940, the literature pertaining to the metrazol treatment and to its different applications has grown to such proportions that the printing of just a list of the references would require several hundred pages. This amazing surge in scientific research and a renaissance of psychiatry I consider the greatest results of the shock treatments.

As to the efficacy of the different methods used to produce convulsions, I feel that through increasing amelioration we have made the convulsive treatment more humane and therefore more tolerable, but that in many cases we have paid for this improvement by a decrease in the quality of the remissions. I received best remissions by the use of camphor. The metrazol convulsions, though much easier to produce, have satisfied my desire for perfect remission somewhat less. And the electric convulsions of de Bini have many times left me with a desire to return to the original camphor convulsions. Not that I deny that these treatments—camphor, metrazol, electricity, picrotoxin, coriamyrtin (Bleckwenn—1940), ammonium chloride (Betoleni—1937)—are physiologically or pharmacologically different. I subscribe to the following statement of Kalinowsky and Hock, who thus introduce their chapter upon the "convulsive therapies" in their book *Shock Treatments, Psychosurgery, and Other Somatic Treatments in Psychiatry:* "Von Meduna introduced convulsive therapy on the basis of theoretical considerations, choosing the pharmacologic provocation of convulsions. However, his method was never meant as a new drug treatment for mental diseases. Its primary object was to utilize the effect which convulsive seizures may have on the schizophrenic disease process. It, therefore, was a logical development when Cerletti and de Bini replaced chemical convulsive agents with electric current. The advantages of this electric convulsive treatment are convincing, but the method should be understood essentially as a technical modification of the original convulsive treatment; again, it was not the electric current that was expected by Cerletti and de Bini to have a therapeutic effect per se."

In the therapeutical convulsions there may be some components, or some component, unfortunately as yet unknown, that are germane to the means by which the convulsions are produced. These components, or this component, as yet unknown, may be nothing other than the severity of the convulsion, which may be the factor responsible for the different qualities of improvements achieved by the different convulsive therapies.

DR. L. J. MEDUNA'S PUBLISHED SCIENTIFIC PAPERS

Brain Histopathology

1. The evolution of the pineal body in infants, Hungarian Med. Arch. 6:1–8, 1924.
2. Die entwicklung d. Zirbeldruse in Sauglingsalter, Ztschr. f. Anat. u. Entwicklungsgeschichte 76:534–547, 1924.
3. Experimentelle B-Avitaminose des Kaninchens, Arch. f. Psych. 80:480–512, 1926.
4. Beitrage zur Histopathologie der Mikroglia, Arch. f. Psych. 82:123–193, 1927.
5. Untersuchungen uber die experimentelle Bleivergiftung beim Meerschweinchen, Arch. f. Psych. 87:571–598, 1929.
6. Effect of neurosmon in treatment of neurosyphilis, M. J. Hungary 74:410–411, 1930.
7. Tuberose Sklerose und Gliom, Ztschr. f.d.ges. Neurol. u. Psychiat. 129:679–712, 1930.
8. Klinische und anatomische Beitrage zur Frage der genuinen Epilepsie, Deutsche Ztschr. f. Nervenh. 129:17–42, 1932.

The Convulsive Treatment

9. Uber experimentelle Campherepilepsie, Arch. f. Psych. 102:333–339, 1934.
10. Versuche uber die biologische Beeinflussung des Abaufes der Schizophrenia. 1. Campher und Cardiazolkrampfe, Ztschr. f.d.ges. Neurol. u. Psychiat. 152:235–262, 1935.
11. Labyrinthreizungsuntersuchungen bei Schizophrenie, Psychiat.-neurol. Wchnschr. 37:26–29, 1935.
12. Die Konvulsionstherapie der Schizophrenia, Psychiat.-neurol. Wchnschr. 37:317–319, 1935.
13. New methods of pharmacological treatment of schizophrenia, Gyógyászat (Hungary), 76:226–227, 1936.
14. New methods of pharmacological treatment of schizophrenia, Arch. Neurol. & Psychiat. 35:361–363, 1936.
15. La Terapia della convulsione nella schizophrenia, Arch. gen. di neurol. psichiat. e psicoanal. 17:289–295, 1936.
16. Die Konvulsionstherapie der Schizophrenie (monograph), Carl Marhold Verlagsbuchhandlung, Halle, 1937.
17. The significance of epileptic fits in shock therapies, Psychiat.-neurol. Wchnschr. 39:331–334, 1937.
18. The Cardiazol Therapy, Lijecnicki Vjesnik 59:1–11, 1937.
19. Allegemeine Betrachtungen uber die Cardiazoltherapie, Schweiz. Arch. f. Neurol. u. Psychiat. 39:32–38, 1937.
20. Significance of convulsive reaction during insulin and cardiazol therapy, J. Nerv. & Ment. Dis. 87:133, 1938.
21. Über die haufigsten Fehler bei der Konvulsionstherapie, Psychiat.-neurol. Wchnschr. 40:87–97, 1938.
22. General discussion of cardiazol therapy, Am. J. Psychiat. 94:40–50, 1938.
23. Il trattamento della schizophrenia negli osp. Rass. di studi psichiat. 27:883–895, 1938.
24. Vierjahrige Erfahrungen mit der cardiazol-Konvulsionstherapie. Psych. en. neurol. bl., Jaargang 1938, No. 5 en 6.
25. Development of cardiazol treatment, Orvosi Hetilap 83:235–257, 1938.
26. Die Konvulsionstherapie der Schizophrenia. Ruckblick und Ausblick, Psychiat.-neurol. Wchnschr. 41:165–169, 1939.
27. MEDUNA AND FRIEDMAN: The convulsive-irritative therapy of the psychoses. Survey of more than 3,000 cases. J. A. M. A. 112:501–509, 1939.
28. MEDUNA AND ROHNY: Insulin and cardiazol treatment of schizophrenia, Lancet 1:1139–1142, 1939.
29. Genese de Traitment de la schizophrénie par la cardiazol, Ann. méd. psych. 97:546–554, 1939.
30. La Therapeutique de la schizophrénie par les convulsions, J. belge de neurol. et de psychiat. 4:227–237, 1939.

31. A Convulsoterapie de esquisophrenia, Rev. méd. brasil *5*:29–36, 1939.
32. Diagnostice da epilepsia, Rev. neurol. e. psychiat. (Brazil) *5*:101–109, 1939.
33. Aralgo mas sobre la terapia convulsivant, Bol. de asilod. alienados en oliva (Argentina), 1939.
34. Meduna and Fox: El Tratamiente convulsivante, Bol. de asilod. alienados en oliva (Argentina) 1939.
35. Meduna and Miskolczy: Teoria de neuronic e neuropathologia, Cult. médica (Brazil) 1939.
36. Common factors in shock therapies, Dis. Nerv. System 6:No. 9, 1945.

Biochemical Disturbances in Schizophrenia

37. Meduna, Gerty, and Urse: Biochemical disturbances in mental disorders. 1. Anti-insulin effect of blood in cases of schizophrenia, Arch. Neurol. & Psychiat. *47*:38–52, 1942.
38. Meduna, Braceland, and Vaichulis: Diagnostic difficulties and levulose tolerance test in "functional" mental diseases, Dis. Nerv. System 6:No. 3, 1943.
39. Dyshormonism in psychoses and its correction by shock, J. Nerv. & Ment. Dis. *98*:No. 5, 1943
40. Braceland, Meduna, and Vaichulis: Delayed action of insulin in schizophrenia, Am. J. Psychiat. *102*:No. 1, 1945.
41. Meduna and McCulloch: The modern concept of schizophrenia, M. Clin. North America, Jan. 1945.
42. Meduna and Vaichulis: A hyperglycemic factor in the urine of so-called schizophrenics, Dis. Nerv. System *9*:No. 8, 1948.
43. Oneirophrenia (monograph), University of Illinois Press, Urbana, Ill., 1950.

The Carbon Dioxide Treatment of Psychoneuroses

44. Pharmaco-dynamic treatment of psychoneuroses, Dis. Nerv. System *8*:No. 2, 1947.
45. Tratamento farmaco dinamico das psiconeuroses, Arq. neuro-psiquiat., São Paulo *5*:No. 3, Sept. 1947.
46. Alterations of neurotic behavior by use of carbon dioxide inhalations, J. Nerv. & Ment. Dis.
47. Meduna and Gyarfas: Motor and sensory phenomena during therapeutical carbon dioxide inhalations, Dis. Nerv. System *10*:No. 1, 1949.
48. A neurophysiological theory of psychoneurosis, J. Nerv. & Ment. Dis. *110*:No. 5, November, 1949.
49. Clinical and biochemical indications of the convulsive and of the carbon dioxide treatments, Herman & Cie, Paris, 1950.
50. Carbon Dioxide Therapy (Monograph). Charles C Thomas, Springfield, Ill., 1950.
51. The carbon dioxide treatment. In The Biology of Mental Health and Disease. Paul B. Hoeber, Inc., New York, 1952.
52. Meduna and Jackman: Carbon dioxide inhalation therapy. In Psychiatric Treatment. Proc. A. Res. Nervous & Mental Dis. Williams & Wilkins, Baltimore, 1953.
53. The mode of action of carbon dioxide treatment in human neuroses, J. Nerv. & Ment. Dis. *117*:January 1953.
54. A modification of carbon dioxide treatment using nitrous oxide, Dis. Nerv. System *14*:No. 4, April, 1953.
55. The physiological background of the carbon dioxide treatment of the neuroses, Am. J. Psychiat. *110*:No. 9, March, 1954.

The Carbon Dioxide Treatment

A REVIEW

*L. J. Meduna, M.D.**

CHICAGO, ILLINOIS

The carbon dioxide treatment, even though we usually do not think of drugs as having a gaseous form, is a pharmacological treatment. During ancient times, and even during the Middle Ages, any drug had to be given in decoction, or in digeratum, or as tea, all of them liquids. Later, probably in the Renaissance, solid forms of medication—such forms as powders, tablets, and pills—were accepted by the lay public as drugs or medicine. Still later, the parenteral administration of medicine through injections came into vogue. Finally, the administration of gases to induce anesthesia was accepted. In the evolution of medication, the next logical development, I think, will be the acceptance of carbon dioxide, and other gases still to be discovered, as legitimate medicaments for treatment for suitable pathologic conditions.

HISTORY

I came upon the use of carbon dioxide in a somewhat roundabout way. As I have mentioned in my monograph, in Budapest in 1934 I heard a garbled report of the work of Loevenhart, Lorenz, and Waters.

At that time I knew no English; and so, being unable to read the original reports, I had to follow the rumors that I gathered. According to these rumors, Loevenhart, Lorenz, and Waters had used oxygen in catatonic conditions by injecting it into the cerebellar cysterna. I carried out a series of experiments in which I similarly injected oxygen, but from these I saw no results. Later, in 1937, an English psychiatrist, a Dr. Cook, informed me that the American authors were using carbon dioxide, which they were administering by having patients inhale it. In 1937 and 1938, I administered carbon dioxide to catatonics and other schizophrenic patients, with results identical with those which Loevenhart, Lorenz, and Waters had obtained: some patients seemed to benefit from the carbon dioxide anesthesia; but their improvement lasted, at most, one-half hour, after which time their catatonic conditions reappeared. This, my early experimentation with carbon dioxide, I discontinued.

In 1942 and 1943, we at the Illinois Neuropsychiatric Institute carried out experiments, first on animals, by injecting cyanide intravenously. The convulsive phenomena following the injection led us to believe that cyanide might be utilized as a variant in the convulsive treatment of schizophrenia. Accordingly, we carried out cyanide-injection experiments on, I believe, about 40 schizophrenic patients, each of whom received a fairly long series of cyanide injections and each of whom responded with an appropriate motor discharge. *None of these patients, however, recovered* from their illness as a result of these convulsions,

* Professor of Psychiatry, University of Illinois College of Medicine.

although an expected percentage of the same patients later recovered with electrically induced convulsions. This fact led us to study cyanide convulsions in greater detail. As it developed, cyanide convulsions are not *grand mal* convulsions, since they are not caused by cortical stimulation and followed by downward discharge from the brain cortex. These convulsions are release phenomena because of the fact that the cyanide inactivates cortical integration and inhibition upon the deeper motor centers; thus the normally suppressed or controlled low-motor-center function appears as motor phenomenon of the body.

During my observations of cyanide convulsions, I developed, tentatively, a theory by which I at first tried to explain why convulsions produced by metrazol, picrotoxin, electricity, etc., have curative effects upon psychotic conditions and why inhibition of higher cortical centers does not have similar curative effects. Basic to this theory were my assumptions that psychotic processes are due to biochemical disturbances in the cortex of the brain, which disturbances are self-sustaining; and that psychoneuroses are disturbances of lower structures of the brain, which disturbances upset or distort the emotional values of the concepts formed in the brain cortex. If, in accordance with the latter assumption, cyanide would effect the lower structures of the brain, then, I further assumed, a profound alteration of the psychopathological symptoms in neurotics might be achieved.

Cyanide, being a powerful and dangerous drug, did not seem suitable for mass experiments. I had to look, therefore, for some other agent which would produce physiological effects similar to those produced by cyanide. Fortunately, at that time I remembered the work of Loevenhart, Lorenz, and Waters; and, to my joy, I found that these authors had experimented with cyanide at about the time when they were working with carbon dioxide inhalations. Thus, by way of a long detour, I was able to continue Loevenhart, Lorenz, and Waters' work by assuming psychoneuroses as a proper indication for this treatment.

METHOD

In developing my method, I made initial mistakes: to my first few patients I gave 100 per cent carbon dioxide to inhale. The results were formidable: massive motor discharges, decerebrate fits on the objective level, and horrifying dream experiences on the subjective level. None of these patients ever permitted a second experiment. One of them, in fact, still in a half-daze, jumped off the treatment table and began to run out of the laboratory at such speed that only at the door were we able to catch him and hold him by force until he had calmed down enough to be permitted to leave the building. After a few of these crude experiments, I made the opposite mistake. I administered 5 per cent to 10 per cent carbon dioxide to a number of patients who were willing to take it; but from the inhalations by these patients I saw no results. After many a trial and error, I arrived at two concentrations of carbon dioxide that I found suitable for the treatment. One was a mixture of 20 per cent carbon dioxide and 80 per cent oxygen; the other, 30 per cent carbon dioxide and 70 per cent oxygen. I could not go any higher with the concentration of the carbon dioxide for the simple reason that no greater concentration than that, mixed with oxygen, can be put under the high pressure necessary, into the tanks. If it were tried, a certain amount of

carbon dioxide would freeze out from the mixture in the form of dry ice, and the gas mixture would still be one of 30 per cent carbon dioxide and 70 per cent oxygen.

The use of 20 per cent carbon dioxide I discarded early; from then on I used the mixture of 30 per cent carbon dioxide and 70 per cent oxygen. This mixture has the great advantage of producing anesthesia without a long transitional phase from full consciousness to narcosis. Furthermore, the mixture can be obtained commercially without difficulty in almost any country. And, finally, this mixture necessitates the use of only one tank and a few gadgets.

The most important of these gadgets is the reducing valve. In this treatment, no reducing valve that limits the flow of gas to 20 or 30 liters per minute can be used. The best kind of reducing valve is that reproduced in figure 1. It has a manometer that shows the pressure of the gas inside the tank and one valve that permits the flow of gas into a rubber tube. This tube is connected with a 10-liter breathing bag, which is connected with the mask. The valve ought to be so constructed as to permit the flow of any amount of gas, depending upon how far the valve is opened. The mask must have an automatic spring valve, or other type of exhaling valve, which opens when the patient exhales and closes when he inhales, thus preventing his rebreathing into the bag.

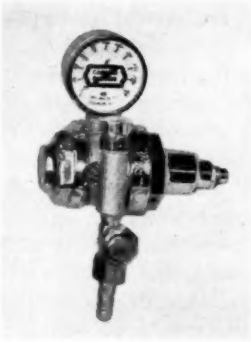


FIG. 1.

When the two mixtures—20 per cent carbon dioxide with 80 per cent oxygen and 30 per cent carbon dioxide with 70 per cent oxygen—had proved to be suitable for treating psychoneurotics, my greatest problem was to minimize any autosuggestion in the procedure—a goal which can to some degree be approached but can never be reached. I told the patients not to expect anything from this treatment because I did not know whether it would work. Furthermore, I depreciated any improvement or change in their conditions which they reported, telling them firmly that these changes had been due only to autosuggestion and that during the further experimentation they would evanesce.

Before the first treatment, I found, some explanation must be given to the patient; but the shorter the explanation, the less was his anxiety regarding the procedure. While the treatment was in the experimental phase, I omitted any allusion to its possible efficacy; but I assured the patient that it was utterly harmless. I told him that the gas would produce a special kind of anesthesia, during which he would sleep; that he would be unable to talk and therefore would reveal no secrets; that he might have a dream during the treatment; and that, although the dream would have no particular significance, he should tell it to me after the treatment was over.

Before giving the treatment, I had the patient remove his shoes, loosen his collar and necktie, and lie down upon a treatment table. After I had opened the valve and when the gas was flowing freely, I put the mask on the face of the patient.

For didactic purposes, we may differentiate three phases of a single treatment: the introductory phase, the anesthesia phase, and the transitional phase. The introductory phase

may last from 1 to 20 or 24 respirations. The length of this phase I determined by asking the patient, after the treatment, the last count he had heard. (While the patient had been taking the gas, I had counted the number of respirations loudly. He usually did not remember more than 8 to 12 counts.) During this phase, the respiratory rate is increased slightly, and the respiratory volume apparently is increased considerably. Flushing of the face and, occasionally, slight perspiration appear.

The phase of anesthesia is characterized by various motor and sensory phenomena. The motor phenomena develop fairly rapidly; there is a little difficulty, therefore, in relating the appearance of these manifestations to the amount of gas inhaled. From about the tenth to the thirtieth respirations, indications of psychomotor excitement are often discernible. Occasionally these indications resemble a struggle to escape discomfort caused by the gas; most often the movements of the patient reveal the nature or the tone of mood accompanying his dreamlike experiences.

During the first 10 to 30 respirations, the lower extremities are often flexed at the hip, and the knee joints are slightly abducted. There are also a slight flexor hypertonus in the upper extremities and, frequently, carpal spasm in both hands. During the interim of 30 to 50 respirations, adversive seizures may occur. These consist of conjugate deviation of the eyes and torsion of the whole body in the same direction, usually with flexion of the legs and extension of the arms on the side toward which the eyes have turned. During these adversive seizures, the pupils react to light. Following or preceding these adversive seizures, rhythmic movements of the legs, resembling those in bicycling, may occur. Commonly, there is simultaneously an alternating change in the tonus of the contralateral upper arms, which movements, together with those of the legs, resemble the movements in quadripedal locomotion. During this phase—i.e., the phase of anesthesia—the pupils are usually dilated, and the reaction to light remains prompt.

Simultaneously with these phenomena, the behavior of the deep and superficial reflexes changes. After 20 to 60 inhalations, appropriate stimuli may provoke forced gasping and biting. After 30 to 40 inhalations, the plantar reflexes become less active; and after 50 to 60 inhalations, these reflexes disappear. At this time, Babinski reflex can be elicited. If the inhalation is continued beyond this phase, a decerebrate fit will ensue; but this fit, I assumed, is beyond the therapeutical range. The patient's recovery from the anesthesia usually occurs promptly—within one or two minutes. After the first treatment, usually the patient is confused; he does not recognize the doctor or the treatment room. But tactful handling with reassuring words help greatly; and the patient, usually with a smile, soon signifies that he has recovered his consciousness and recognizes the doctor.

The sensory experiences of the patients during the administration of carbon dioxide are intriguing. I usually call these phenomena dreams, although they do not fit into the category of dreams, hallucinations, or delusions. These sensory experiences may consist of only the three groups of form-constants described by Klüver. The first of these constants Klüver had designated as grating, lattice, fretwork, filigree, honeycomb, or chessboard design. A form-constant related to these is the cobweb figure, which my patients saw as cobwebs, spokes of a giant wheel, converging lines, and streets of huge dimensions. His

second form-constant Klüver designated by such terms as tunnel, funnel, cone, and vessel. During the carbon dioxide anesthesia, the patients may feel motionless, and the revolving tunnel engulfs them. The third form-constant of Klüver is the spiral. This form is frequently reported by the CO_2 patients; they have approached a spiral, or a spiral has approached them, or they have felt that they are in the axis of a huge spiral.

A fourth constant of these sensory experiences I have described and named *dynamic-constant.* This constant has been described by my patients specifically. They have seen dots *falling* down in a constant rain or geometric figures sometimes *approaching* them, some of these figures moving on a horizontal plane, others *undulating*, and still others *gyrating* from the center toward the periphery.

Whether these visual and dynamic phenomena correspond to a stimulation of the visual cortex or to the stimulation of some other part of the brain, I cannot say. Some psychosensory experiences of a higher order seem to point to the stimulation, or to the independent function, of the temporal lobes. One of these psychosensory experiences of a higher order is a frequently reported *déjà vu*, which is recognized as a temporal lobe symptom.

Another of these psychosensory experiences is the phenomenon that has been described by Klüver and called by him *presque vu*. This phenomenon is characterized by an event or a visual image pointing in a certain direction, the suggested end of which is not quite reached. Or this phenomenon lacks the proper completion; it does not call forth a "closure" experience. A form, a movement, a pattern, etc., is almost complete; but, since it is never completed, a characteristic *presque vu* experience arises. The *presque vu* sensation may be adjectival to a problem—a problem spiritual, philosophical, or mathematical. To the *presque vu* sensation may be attributed a "special" or "cosmic" importance, as if the sensation were of esoteric importance, individual or cosmic—as if it had a function of divination. The *presque vu* sensation may be carried by any of the constants or may present itself in purity.

Another sensory phenomenon that commonly accompanies the CO_2 treatment is that which I have described under the name of *experience revenant.* This phenomenon may appear several hours or several days after the treatment. It comprises one of two kinds of experience: a sudden remembrance of a sensory phenomenon experienced during the actual CO_2 therapy, or just a feeling that the patient is taking the CO_2 treatment.

Besides the visual type of sensory symptoms, the patient may experience auditory, somaesthetic, or rarely olfactory sensations. Any one of these sensations may develop into a complex dream. In such a dream, one patient saw eccentric rings of blue and yellow suspended from the center. These began to undulate, forming a funnel. The yellow rings appeared and began to wave; and the whole scene turned into a seascape of deep blue with an ultramarine sky and a vibrating yellow light. Another patient saw a circle of light which grew immense and then became a wheel. The patient was the hub; the spokes were made of figures, which represented some planning for which he was responsible. Sometimes in the center of the visual field distant small objects appear and begin going faster and faster, *growing* as they move outward. Sometimes, also, patients have reported micropsias, or a feeling of being small.

When the visual sensations develop into dreams, they often possess strong catathymic components. These dreams are strange, even weird, in a way that sets them apart; they are like some epileptic auras or ecstatic experiences. One normal experimental subject has thus described a dream experience: "I had an impression of being in complete understanding and harmony with God. Seemed like an abrupt awakening of truths I should have known but somehow didn't before. Failures and successes faded into insignificance and I was possessed with an all-consuming Love—so strong and intense and beautiful—everything was right—always had been right. Only human's thoughts, errors, and miscomprehension of the plan distorted facts and made the misery and unhappiness that is part of our lives. In my dream, the latter part of it, my thoughts seemed to disconnect from the divine harmony and I had to struggle to keep from turning the entire experience into a nightmare."

All these sensory phenomena—dreams, hallucinations, *presque vu*,—rest, I am convinced, on some underlying physiologic function of some brain structures, which function operates independently of what, in psychiatry, we call personality. Furthermore, any one of these phenomena, I am convinced, can be secondarily invaded and modified by the psychologic problems and other troubles of the individual.

As to the number of treatments necessary to be administered to a patient—necessary, i.e., for a cure—it is difficult to give instructions. I administer, usually, three treatments a week, one every other day. I prepare the patient not to expect any sign of improvement at the beginning. If, however, after some 20 treatments, he has not reported any improvement, I terminate this procedure and recommend another. The number of treatments that I have administered in successful cases has varied from about 15 to about 200.

MODIFICATIONS OF THE ORIGINAL METHOD

The great difficulty that one encounters in the treatment of anxiety cases with CO_2 is due to the fact that CO_2, since it affects the medulla and produces hyperventilation, may, in the beginning, increase the patient's anxiety. To remove this difficulty, I modified the CO_2 treatment by using nitrous oxide to introduce anesthesia. The apparatus that I set up for doing so is shown in figure 2. The tank of 100 per cent nitrous oxide and the other tank of 30 per cent carbon dioxide and 70 per cent oxygen are connected by a single tube, which leads to the breathing bag. In this combination, I do not mix the two gases; but, after first opening the nitrous oxide, I apply the mask to the patient's face and let him inhale this gas for 20 to 60 seconds. Under no circumstances should the nitrous oxide be given longer than 60 seconds because it is a more dangerous gas than CO_2 and because during its administration an anoxemic state of the brain develops. During the administration of the nitrous oxide, I talk to the patient, asking him such questions as: "Are your legs numb?" "Is your face numb?" "Do you still hear me?" During this questioning, I do not lift the mask from the patient's face; his voice is audible through it.

When the patient is unable to answer verbally, I consider the anesthesia deep enough to switch over to the administration of CO_2. And so, without removing the mask from the patient's face, I close the nitrous oxide valve and turn on the CO_2. From then on, counting

the respirations of CO_2, I give the required number, usually 20 to 30. Since I introduced this modification of the treatment, I have hardly ever begun the treatment of a patient with a straight administration of the CO_2 mixture; but, for the first 10 or 20 treatments, I have used the nitrous oxide modification. After about 14 to 20 of these treatments, the patient's anxiety has so decreased that I try the administration of the CO_2 mixture without the nitrous oxide introduction. If the patient objects to this straight administration of the CO_2, I do not insist upon using it; many times I have used the nitrous oxide-carbon dioxide combination from the beginning until the termination of the treatment.

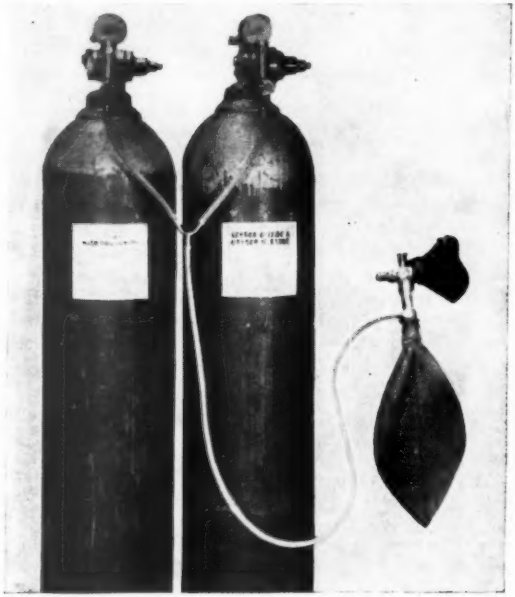


FIG. 2

My nitrous oxide combination with the carbon dioxide treatment was not, however, the first published modification of my original technique. My original method of administering the carbon dioxide treatment has undergone many other changes, changes initiated by eager research men who have wanted to improve the original method and thus achieve a greater number of recoveries. These modifications I shall designate, for the time being, by the names of those who first introduced them into the treatment.

The first of these modifications to have been published is that of P. Wilcox, who has modified the original therapy by combining carbon dioxide treatment with psychotherapy. His technique, which he has termed "psychopenetration," consists of administering 5 to 10 respirations of carbon dioxide and then asking the patient certain key questions to test the accessibility of the latter's unconscious conflicts.

The modification next published is that which has been worked out by W. Liddell Milligan of Portsmouth, England, and, I believe independently of him, by W. Sargant of London. Milligan has written:

> It occurred to me that more use might be made of the "subcortical excitatory state" described by Meduna, and that it should not be necessary for the patient to lose consciousness. The following modified technique was therefore worked out. The patient receives treatment in bed in a quiet room and the procedure is briefly explained. It is emphasized that consciousness will not be lost and that after inhaling the gas he is to "let himself go" and do and say exactly what he wants. It is useful to spend some time in insuring that the patient knows what is required of him. A Boyle anesthetic apparatus is used and the patient is first allowed to inhale

pure oxygen, the mask being held a few inches above the face and gradually lowered into position. . . . After a few respirations, carbon dioxide is gradually introduced until 10 to 15% is being given. After 20 respirations the amount of carbon dioxide is increased to 30%, and then almost immediately lowered to the former level. The inhalation is terminated rapidly after 25 to 40 respirations. . . . As soon as the mask is removed the nursing staff retires, but should be within call lest any subsequent violence ensues. Some patients abreact immediately, but others recount former incidents for as long as half an hour before any true release of emotion takes place. It is necessary for the psychiatrist to devote at least an hour to each patient and to be content to await results. It is only rarely necessary to encourage the flow of material. When, however, abreaction occurs, it is helpful to increase the drama and attain the emotional atmosphere.

J. D. Moriarty of California has combined the classical carbon dioxide therapy with psychotherapeutic technique. Moriarty's finding:

Carbon dioxide therapy facilitates treatment by brief analytical methods through which the experienced therapist may usually uncover rather quickly the infantile trends that generally constitute the core of a neurosis. . . . Development of the transference situation is hastened by carbon dioxide therapy, and both positive and negative phases more easily worked through. Sometimes a patient who is unaware of his hostile feelings for the therapist is greatly surprised when these rise suddenly to the surface, as he emerges from the carbon dioxide coma, yet as he regains full consciousness 30 or 40 seconds later he retains sufficient memory of these negative feelings to be able to discuss them with much more therapeutic gain than at first. Occasionally the patient becomes flooded with a rush of hitherto buried feelings that disturb him considerably. At such times the therapist may find it advisable to give him another treatment in short order to dissipate this particular reaction. As skill in the technique develops it becomes possible to achieve therapeutic gains of the fundamental nature that equal or surpass those of the painfully slow and protracted psychoanalytical technique of traditional procedures.

A. A. LaVerne has worked out another modification of the carbon dioxide treatment, one which he has described under the name of "rapid coma technique." In this technique, LaVerne mixes a gas of 70 per cent carbon dioxide and 30 per cent oxygen in a 10-liter breathing bag and administers to the patient a single deep maximal inhalation. He has reported:

When the patient gives a signal that he cannot inhale any more gas, the mask is quickly removed. At that time the patient is still fully conscious. He then rapidly enters a carbon dioxide coma, or sub-coma, or hypnagogic state, during which he almost invariably visualizes a geometric, colorful pattern with or without formed symbols. Within a matter of 8 seconds he is fully awake and recalls every detail of the treatment. In the meantime he demonstrates autonomic and motor body reactions consisting of skin changes, perspiration and flushing, mottling, motor activity and vocalizes without the usual severe exhaustion that follows the multiple breath technique of prolonged carbon dioxide.

LaVerne usually gives three treatments a week, treatments in which he administers 1 to 10 single-breath inhalations and allows between these inhalations intervals of at least three minutes. "Psychotherapy," he says, "may be utilized between treatments if the physician so desires." If, after three or four weeks, this schedule has not produced clinical improvement in the patient, LaVerne, considering that intensive treatment is then required, gives the patient up to 20 single-breath treatments daily for a period of two weeks.

LaVerne has developed a variation of his single-breath technique by using repeated inhalations of high concentrations of carbon dioxide. In this technique, he induces anesthesia by giving nitrous oxide to the patient; after anesthesia has been reached, he ad-

ministers from 4 to 12 respirations of a 90 per cent to 95 per cent carbon dioxide–10 per cent to 5 per cent oxygen mixture. His best therapeutic results, he claims, he obtains with six to nine breaths of this mixture. "The criterion for the optimum number of breaths is the production of physiological level of coma, with mild twitchings or mild clonic movements of face and body, lasting approximately 10 to 15 seconds. The therapist should avoid production of a deep generalized convulsive level unless the most superficial levels of coma have been ineffective after a preliminary trial of 5 to 10 treatments."

A. I. Jackman was the first to utilize the CO_2 treatment to produce therapeutic convulsions. In his technique, which he calls "carbon dioxide convulsive treatment," he utilizes carbon dioxide inhalation to a point of convulsive reactions in depressed patients who have not reacted quickly to the original carbon dioxide-inhalation therapy. He uses my original method and my nitrous oxide combination but modifies these by continuing with the carbon dioxide inhalation to the point at which the patient develops what could be described as a decerebrate fit.

W. E. Wilkinson also utilizes the CO_2 treatment to produce therapeutic convulsions.

> We have used convulsive CO_2 therapy on patients who previously would have been given convulsive electroshock therapy. This group has included patients with schizophrenia, obsessive-compulsive neurosis and those with the manic and agitated depressed phases of manic depressive psychosis. These patients have shown tremendous variations in their convulsive threshold and in the intensity and duration of the convulsions. Following the CO_2 induced convulsions, the patients go through the several stages of the awakening reaction not unlike patients recovering from electric convulsive therapy. Patients who have been treated by this method usually have shown temporary relief of symptoms immediately after the treatment, but in most of them the improvement has not lasted for as long as 24 hours. A few patients have been completely relieved of their symptoms, but all of these were treated in 1952 and we do not know how permanent the relief will be

W. M. C. Harrowes of Scotland and Z. Selinger of Canada, having reached the same conclusion independently, have achieved beneficial results by giving only 5 to 10 respirations of the 30 per cent carbon dioxide–70 per cent oxygen mixture and thus not producing any anesthesia. The administration of this limited number of respirations they repeat five to ten times during one treatment. The time between the repeated administrations of the gas they use for psychotherapy. Their modification of my original technique they call the "fractional method of carbon dioxide therapy." This method, apparently, can be used only in selected cases.

INDICATIONS

As is well known, it is extremely difficult to construct any adequate classification for the psychoneuroses. Our present-day classifications are more or less descriptive. In my "Alterations of Neurotic Pattern by Use of CO_2 Inhalation," I have listed stuttering, spastic colitis, anxiety neuroses, a feeling of inferiority, irritability, neurotic fatigue, alcoholism, homosexuality, and other character neuroses that are amenable to the carbon dioxide treatment. At the time of the publication of this article, I had not had any success with obsessive-compulsive neuroses and psychoses.

LaVerne claims that with high concentrations of CO_2—concentrations up to 95 per cent

—he has achieved results in some cases of schizophrenia; but as to the efficacy of LaVerne's method in psychoses, no useful statistics are available.

Douglas MacRae has introduced the CO_2 treatment into obstetrics, where he uses it both during the pregnancy, in order to treat anxiety about delivery, and during labor, as an analgesic. He claims that "during pregnancy the CO_2 treatments were helpful in controlling the vomiting of pregnancy, insomnia, or unusual nervousness."

G. A. Silver, who has used the CO_2 treatment on a fairly large group of psychoneurotics, has succeeded in curing a woman of 40 "hysterically blind for eight years, who received a pension on the basis of her blindness." Silver has found, furthermore, that while psychoneurotic depressions respond favorably to CO_2 treatment, "it seems valid to make a distinction from the manic-depressive patients, which do not seem to be favorably affected by the CO_2-O_2 treatment."

Leonard J. Liest has found CO_2 therapy to be useful in the treatment of psychotic patients after remission has been produced by the use of shock therapies.

Temple Fay claims good results with inhalations of 20 per cent CO_2-80 per cent O_2 in patients suffering from "true types of rigidity" (parkinsonism and athetosis). Confirmation of his claims is lacking.

A. A. LaVerne claims excellent results in chronic alcoholism if he initiates the course of CO_2 therapy for the alcoholic in a hospital for at least 50 treatments. After giving these 50 treatments, he discharges the patient and puts him on a once-a-week maintenance schedule.

Anna May Smith, who has treated stutterers with the carbon dioxide therapy, has found that 21 of her 33 patients were improved—that 11 showed 100 per cent improvement; 3, 75 per cent; 2, 50 per cent; and 5, 25 per cent.

Jackman reports success with CO_2 treatment in patients with allergy, such as hayfever and asthma.

CONTRAINDICATIONS

Contraindications for the CO_2 treatment are few; and these have been arteriosclerosis, hypertension of high degree, diseases of the heart muscle, coronary disease or attacks, and advanced emphysema. Psychiatric contraindications were first published by Simms et al, who have stated that "pre-psychotic states were found to be precipitated into open psychoses as a result of these treatments."

Inasmuch as we do not have any test or method that would determine the degree either of a neurosis or of its improvement or cure, for the purposes of this presentation I shall omit the word "cure" from my statistics and designate the results in terms of "improved" and "not improved" groups (Table I).

That these statistics are somewhat misleading is apparent to everybody who has an understanding of statistical principles and has been working with psychoneurotic patients. These figures give an erroneous impression because of the fact that the degree of improvement for the time being cannot be measured; therefore, patients slightly improved, improved, greatly improved, and cured are grouped as "improved" patients. These statistics, furthermore, are incomplete because many authors mentioned in their reports "large" numbers of pa-

TABLE I

	Improved	Not Improved	Total
Meduna	208	112	320
Kindwall	45	55	100
MacRae	31		31
Milligan	40		40
Pellage	7	3	10
Silver	39	11	50
Weaver *et al.*	8	5	13
Jackman and Schorr	8	2	10
Moriarty	62	12	74
Silver	174	76	250
LaVerne and Herman	35	15	50
A. M. Smith	21	12	33
Simms *et al.*	38	34	72
	716	337	1,053

tients whom they had treated, but referred in their statistics to only small numbers; and because other authors merely published that they had treated 30 or 40 patients with excellent results and presented three or four representative case histories, without giving statistical analyses of their whole groups. These statistics, however, cannot fail to convey to the unprejudiced reader the impression that the treatment is effective in different forms of neuroses. Of 1,053 published cases in which the CO_2 treatment has been used, 716 patients (68 per cent) have improved, and only 337 (32 per cent) have remained unimproved. This 68 per cent—a figure arrived at from computing the results of 13 authors who have treated over 1,000 cases—is interestingly identical with the over-all improvement that I published in my monograph, *Carbon Dioxide Therapy:* "Of the 100 patients, 58 were males and 42 were females. Thirty-six of the 58 male patients—that is, 62 per cent—and 32 of the 42 female patients—that is, 76 per cent—have improved from the CO_2 treatment. The over-all improvement is, therefore, that of 68 out of 100, or 68 per cent of all the cases treated."

TOTAL FAILURES

A few authors have reported total failure in their use of the CO_2 treatment. The reasons would be interesting—if I were able to trace them—for the total failures of some authors as compared with the excellent results achieved by others. Determination of the reasons for these failures is possible, however, in only a few cases. One of these cases is that of Jackson A. Smith, who treated 33 patients with anxiety, hysteria, and depression. Of this group, Dr. Smith has reported, "4 patients responded promptly and sustained their improvement. Eight patients showed slight and usually temporary improvement over a period of 6 to 8 weeks. . . . Twenty-one of the 33 patients received no appreciable help from this method of treatment and in this series the procedure was considered to be of limited value."

The failure of the CO_2 method in Dr. Smith's hands is due to the fact that he apparently did not apply this treatment in a technically correct way. "Six of the patients," he says, "regularly lost consciousness as judged by their failure to recall the last few numbered inhalations." All the authors who have worked out a modification of the CO_2 treatment have agreed that loss of consciousness—that is to say, anesthesia—is an absolutely necessary factor in producing results with the treatment. Doctor Smith's failure to produce anesthesia in about 80 per cent of the cases which he treated explains his meager results and does not controvert the effectiveness of the CO_2 therapy.

The reader must be reminded that Harrowes and Selinger have been using the fractional method of CO_2 therapy, a method that does not produce coma, *in selected cases only;* and that they have been combining this method with psychotherapy.

Hargrove, Bennett, and Steele, who treated 50 patients with anxiety, obtained 17 improvements; but 33 patients did not improve at all. In contrast, they have reported, of 50 patients with anxiety whom they treated by psychotherapy only, 14 recovered, 26 improved, and only 10 showed no change. Their final conclusion is that more patients improved from psychotherapy alone than from a combination of CO_2 and psychotherapy. The shortcoming of these authors' work was that in anxiety patients they used straight CO_2 instead of the nitrous oxide-carbon dioxide combination. Thus, in many cases they increased the patient's anxiety and, furthermore, produced abreactions of such magnitude that the psychotherapist could not appropriately deal with them. By using the nitrous oxide-CO_2 combination and by giving lesser amounts of CO_2, they could have produced abreactions of smaller magnitude, which could have been easily handled by the psychotherapist or by the patients themselves.

Arthurs et al treated 14 stutterers with a combination of nitrous oxide and CO_2. None of these patients recovered from stuttering, nor did their speech improve. With the lack of description of the procedure of these authors, it is impossible to conjecture the cause of their absolute lack of success.

MODE OF ACTION OF THE CO_2 THERAPY

The effectiveness of the CO_2 therapy may be explained by (1) the doctor-patient relationship, (2) autosuggestion and other psychological processes, or (3) physiological effects of the gas upon the whole organism. I cannot help feeling that any explanation that attributes the effectiveness of this therapy to an improved doctor-patient relation or to transference, autosuggestion, abreaction, and other so-called "psychological" processes is no explanation whatsoever, but only a simple description of how the doctor thinks of his work and himself. And his mode of thinking is conditioned by the frame of references which he has obtained through his previous education. Moreover, even if any of the so-called "psychological" explanations that I have designated are partly or wholly acceptable, the physiological basis of the "psychological" explanation should be given in terms of the brain tissue and its function. I do not want to minimize the so-called psychological effects of any treatment situation; but we ought to know that beyond or beneath any psychological function there is the function of the brain, and that unless we can explain our work in terms

germane and applicable to the tissue of the brain and to its function, although we may have described a process, we have not explained it at all.

It was known for some time that CO_2 raises the threshold of stimulation of the excised nerve cell, increases its membrane potential, and, finally, increases the ability of the nerve to conduct trains of impulses. It was known, also, that CO_2 delays the appearance of fatigue of the stimulated nerve. Because of recent researches, we now know more of the action of CO_2. Seifritz has found that CO_2 changes the state of protoplasm from sol to gel; that if the concentration of the CO_2 is too high, or if the exposure to it is too long, the sol-to-gel conversion becomes irreversible. Dusser de Barenne, McCulloch, and Nimms have found that the increased acidity of the brain tissue caused by CO_2 is associated with low electric activity and a decreased excitability of the cortex. McLellan and Elliott have found that CO_2 destroys acetylcholine by lowering the *p*H in the brain. All these effects revealed by recent researches amount to a decreased activity, or a resting state, of the nervous system saturated by CO_2.

From recent researches we have learned of other effects of the action of CO_2 upon the nervous system. Bain and Klein have ascertained that CO_2 enables the brain more clearly to balance energy demands with oxidative processes. K. E. Schaffer has found that if experimental animals are exposed to CO_2, hypersecretion of epinephrine occurs, and that this hypersecretion of epinephrine is followed by hyposecretion, the latter due to a diminished synthesis. Schaffer has found, too, that as an effect of the CO_2 there is a hyper- and a subsequent hypo-phase in the adrenal cortex and in the basophilic cells of the pituitary gland, and that the thyroid gland becomes somewhat inactivated. Pollock, Stein, and Gyarfas have found that CO_2 inhalation produces low-amplitude, fast cortical activity; and that the response of the thalamus to CO_2 is much less than that of the cortex, as is the hypothalamic response, which shows lower-than-cortical amplitudes and slower frequencies.

The data that I have just cited indicate the following trend: (1) increased cerebral inhibition that is repeated in the cortex of the brain at every treatment; (2) decreased excitability of the cortex that is reproduced by every treatment; (3) an effect of the CO_2 upon the carbohydrate metabolism of the brain, enabling it more clearly to balance energy demands with the oxidative process; (4) a changed balance in the activity of the pituitary, adrenal, and thyroid glands. If this biochemical trend is pertinent to the fact of psychoneurosis, it follows that a psychoneurotic's brain structure is hyperirritable; and either that the psychoneurotic's brain does not balance energy demands with oxidative processes properly, or that there is a disturbance in the distribution of this process. Finally, we may assume that there is some disturbance in the interaction of at least three important glands—the pituitary, the adrenal and the thyroid glands. These disturbances that appear on the perceptual level to the patient and to the doctor as disturbances of the mind or as psychosomatic symptoms are rectified by the action of CO_2.

On the phenomenological or clinical level, three modes of improvement resulting from the CO_2 treatment are discernible in the patients. Observations of these different modes will lead many a research man to believe that the improvements move exclusively on the

psychological level and thus forget that no "psychological" way of improvement is possible unless it is based on cortical, neuronal, or glandular changes.

The first and most frequent clinical mode of improvement during CO_2 treatment is manifested by simple diminution and disappearance of the psychoneurotic symptoms. The patients who experience this mode of improvement show decreased emotionality and decreased sensitivity to internal and external stimuli. These changes are apparent in a decrease in and, later, a disappearance of exaggerated reactions, in improved psychological economy, and, sometimes, in considerable changes in physiological activities. Reduction of frigidity in women, normalization of sexual activity in men, improvement in the texture of skin, nails, and hair, increase in the size of the female breast, disappearance of menstrual cramps, and normalization of the menstrual cycle are common changes in the improved cases.

The second mode of improvement during CO_2 treatment occurs through what appears as abreaction. There are three varieties of abreaction. One is the known realistic abreaction, during which the patient relives a previous experience and discharges, or acts out, pent-up emotions. This variety of abreaction occurs in full consciousness and is recoverable by the patient. A second variety of abreaction, and one which I have observed frequently, I call allegoric abreaction. In this, the patient discharges realistic emotions; but these are connected not with a recovered memory but rather with a symbolic dream. This variety of abreaction is recoverable by the patient, but its real meaning remains hidden unless it is explained to him. A third variety of abreaction is utterly unconscious, inasmuch as it occurs when the patient is in the anesthesia phase of the CO_2 treatment. This variety of abreaction is manifested by the patients having, upon awakening, but a vague memory of some unpleasant experience.

The third mode of improvement during CO_2 treatment is the rarest but the most fascinating one. This mode of improvement I call "spontaneous analysis of the patient and reintegration to a more normal personality pattern." The patient who experiences this mode of improvement may not show any considerable emotional discharge and may or may not have either a symbolic dream, or a vague recollection of some past experience during his dream. Later in the day, however, or a few days after the treatment, he recollects forgotten or repressed childhood memories and other pathogenic experiences and discovers the causal relation of these memories and these other pathogenic experiences to his actual symptoms. As the treatment proceeds, he recovers more and more of this material, and the pathologic symptoms correspondingly decrease or disappear.

It would be an error on the part of the therapist to force any one of the above modes of improvement upon everyone of his patients. It seems that some inherent quality of the brain is the factor that will determine the mode of improvement to be followed by the individual patient. If the therapist notices that a patient is inclined, for instance, to produce realistic or allegoric abreaction, he had better switch over to Milligan's and Sargent's abreactive technique, which I have described; on the other hand, there is no use in forcing abreactions upon a patient whose brain has chosen the modality of improvement which I have described as "simple diminution and disappearance of the symptoms." The patient should not be expected to adopt and to adjust himself to any particular method of admin-

istration of the CO_2 treatment chosen or preferred by the therapist. Contrariwise, in order to adjust the technique to the need of the patient, the therapist should use the CO_2 treatment and its modifications as flexibly as he is capable of doing.

Strange as the pharmacological method of the CO_2 treatment may seem, I feel that it has not come to us unheralded. May I remind the reader of one of the last works of Sigmund Freud, *Outline of Psychoanalysis*, first published, in German, in 1940. In this little book, Freud, speaking of the failures of psychoanalytical technique, states: "It is true that we do not always succeed in winning but at least we can usually see why it is that we have not won. Those who have been following our discussion only out of therapeutical interest will perhaps turn away in contempt after this admission. But we are here concerned with therapy only insofar as it works by psychological methods; and for the time being we have no other. *The future may teach us how to exercise a direct influence, by means of particular chemical substances, upon the amounts of energy and their distribution in the apparatus of the mind. It may be that there are other undreamed of possibilities of therapy.*"

The first of these "undreamed of possibilities of therapy," possibilities of influencing "the amounts of energy and their distribution in the apparatus of the mind" by administration of carbon dioxide, I offer to those psychiatrists who have the vision and the courage to follow a still-unbeaten path.

REFERENCES

(Listed according to date of publication)

1. Loevenhart, A. S.; Lorenz, W. F., and Waters, M.: Cerebral stimulation, J. A. M. A. *92*:No. 11 (March 16) 1929.
2. Heinbecker, P.: Effect of anoxemia, carbon dioxide and lactic acid on electrical phenomena of myelinated fibers of the peripheral nervous system, Am. J. Physiol. *89*:58 (June) 1929.
3. Leake, C. D.; Guedel, A. E., and Botsford, M. E.: The stimulating effect of carbon dioxide inhalations in dementia praecox catatonia, California & West. Med. *31*:20 (July) 1929.
4. Kaufman, M. R., and Spiegel, E. A.: Experimentelle Analyse der Beeinflussung katatoner Zustande durch Einatmen von Kohlensäure-Sauerstoffmischungen, Ztschr. f. d. ges. Neurol. xu. Psychiat. *127*:312–320, 1930. (Experimental analysis of modification of catatonic states by inhalation of carbon dioxide and oxygen mixtures.)
5. Leake, C. D.; Wood, D. A.; Botsford, M. E., and Guedel, A. E.: The effects of the administration of carbon dioxide and oxygen in catatonic dementia praecox, Anesth. & Analg. *9*:62 (March-April) 1930.
6. Necheles, H., and Gerard, R. W.: Effect of carbon dioxide on nerve, Am. J. Physiol. *93*:318 (May) 1930.
7. Lasche, P. G., and Rubin, H.: Carbon dioxide-oxygen inhalations in catatonic dementia praecox, U. S. Vet. Bur. M. Bull. *6*:1037–1041 (Dec.) 1930.
8. Heinbecker, P., and Bishop, G. H.: The effect of anoxemia, carbon dioxide and lactic acid on electrical phenomena of myelinated and unmyelinated fibers of the autonomic nervous system, Am. J. Physiol. *96*:613 (March) 1931.
9. Cobb, S., and Fremont-Smith, P.: The cerebral circulation. XVI. Changes in the human retinal circulation and in the pressure of the cerebro-spinal fluid during inhalation of a mixture of carbon dioxide and oxygen, Arch. Neurol. & Psychiat. *26*:731 (Oct.) 1931.
10. Kelman, H.: Observations in catatonia with mixtures of carbon dioxide and oxygen, Psychiatric Quart. *6*:513 (July) 1932.
11. Bennett, C. R.: Carbon dioxide and oxygen in the treatment of schizophrenia, Delaware State M. J. *5*:85 (April) 1933.

12. Campbell, J. M. H., and Poulton, E. P.: Oxygen and Carbon Dioxide Therapy, Oxford University Press, 1934.
13. Schmidt, C. F., and Pierson, J. C.: The intrinsic regulation of the blood vessels of the medulla oblongata, Am. J. Physiol. *108*:241 (April) 1934.
14. Schmidt, C. F.: The intrinsic regulation of the circulation in the hypothalamus of the cat, Am. J. Physiol. *110*:137 (Nov.) 1934.
15. Schmidt, C. F.: The intrinsic regulation of the circulation in the parietal cortex of the cat, Am. J. Physiol. *114*:572 (Feb.) 1936.
16. Dusser de Barenne, J. G.; McCulloch, W. S., and Nims, L. F.: Changes of hydrogen ion concentrations of the cerebral cortex, Proc. Soc. Exper. Biol. & Med. *36*:462 (May) 1937.
17. Dusser de Barenne, J. G.; McCulloch, W. S., and Nims, L. F.: Functional activity and *p*H of the cerebral cortex, J. Cell. & Comp. Physiol. *10*:277 (Oct.) 1937.
18. Gibbs, F. A.; Williams, D., and Gibbs, E. L.: Modification of the cortical frequency spectrum by changes in carbon dioxide, blood sugar, and oxygen, J. Neurophysiol. *2*:49 (Jan.) 1940.
19. Locke, A., and Cohen, M. A.: Effect of inhaled carbon dioxide in rheumatoid (atrophic) arthritis, Proc. Soc. Exper. Biol. & Med. *43*:611, 1940.
20. Moussatche, H.: Effect of high carbon dioxide concentrations on experimental convulsions, An. Asoc. quím. brasil *2*:80, 1943.
21. Craig, F. N.: The effect of carbon dioxide tension on the metabolism of cerebral cortex and medulla oblongata, J. Gen. Physiol. *27*:325–338 (March) 1944.
22. Moussatche, H., and Mello, M. I.: Lactic acid and the inhibition by carbon dioxide of the production of convulsions by application of strychnine to the cerebral cortex, Rev. brasil. de biol. *4*:103 (April) 1944.
23. Palmer, H.: Abreactive techniques—Ether, J. Roy. Army M. Corps *84*:86, 1945.
24. Cohen, M. A.: Inhalation of carbon dioxide in rheumatoid arthritis, M. Rec. 159–155, 1946.
25. Palmer, H.: Pain: its investigation by means of the diagnostic use of ether in neuropsychiatry, Reprinted from the Royal College of Physicians Pamphlet, Sept. 1946. Digest Neurol. & Psychiat., Inst. of Living, *16*:538.
26. Meduna, L. J.: Tratamento farmaco dinamico das psychoneuroses, Arq. neuro-psiquiat., São Paulo *5*:No. 3, 1947.
27. Lorente de No, R.: Stud. Rockefeller Inst. M. Res. 131–148–194, 1947.
28. Meduna, L. J.: Pharmaco-dynamic treatment of psychoneuroses (a preliminary report), Dis. Nerv. System *8*:No. 2, 1947.
29. Wickwire, G. C., and Krouse, R.: The effects of carbon dioxide on insulin convulsions and brain potential, Federation Proc. *6*:226 (March) 1947.
30. Banyai, A.: Fifteen years' experience with carbon dioxide in the management of cough, Current Med. Dig. June, 1947.
31. Baudoin, A.; Remond, A., and DeLarue, R.: Therapeutic effects of inhalation of a mixture of 70% oxygen and 30% carbon dioxide (Carbonarcosis), Bull. acad. nat. méd. *131*:(July) 1947.
32. Mackensen, Otto: Effect of carbon dioxide on initial oviposition of artificially inseminated and virgin queen bees, J. Econ. Entomology *40*:344 (Oct. 22) 1947.
33. Consolazio, W. V.; Fisher, M. B., et al.: Effects on man of high concentrations of carbon dioxide in relation to various oxygen pressures during exposure as long as 72 hours, Am. J. Physiol. *151*:479–503 (Dec. 1) 1947.
34. Wilcox, P. H.: Psychodynamic facilitation with gas anesthetics. In Chap. 33, Shock Therapy (Spiegel, E. A., ed.): Progress in Neurology and Psychiatry, Vol. 3. Grune & Stratton, New York, 1948, pp. 586–7.
35. Pollock, G. H.: Central Actions of Carbon Dioxide. Thesis, University of Illinois, 1948.
36. Meduna, L. J.: Alterations of neurotic patients by use of carbon dioxide inhalations, J. of Nerv. & Ment. Dis. *108*:1948.
37. Psychotherapy aided by Meduna's carbon dioxide treatment, J. Mich. State Med. Soc. *47*:(Jan.) 1948.

38. Bain, J. A., and Klein, J. R.: Effect of carbon dioxide concentration of brain lactate, Federation Proc. 7:145 (March) 1948.
39. Klein, J. R., and Bain, J. A.: Effect of carbon dioxide concentration on the changes in brain metabolites accompanying convulsions, Federation Proc. 7:164 (March) 1948.
40. Shanes, A. M.: Metabolic changes of the resting potential in relation to the action of carbon dioxide, Am. J. Physiol. *153*:93–108 (April) 1948.
41. Sargent, W.: Some observations on abreaction with drugs, Dig. Neurol. & Psychiat. Inst. of Living *16*:193–206 (April) 1948.
42. Gellhorn, E., and Heymans, C.: Differential action of anoxia, asphyxia, and carbon dioxide on normal and convulsive potentials, J. Neurophysiol. *11*:261–73 (May) 1948.
43. Kindwall, J. A.: CO_2 as mental treatment, Science News Letter, May 29, 1948.
44. Ausherman, H. M.: Misconceptions regarding use of carbon dioxide in treatment of respiratory depression and asphyxia, Anesth. & Analg. *28*:172 (May-June) 1948.
45. Baudoin, A.; Remond, A., and Delarue, R.: L'aspect electrique de cerveau au cours de la carbonarcose, Absts.: Rev. neurol. *80*:615–616 (Sept.-Oct.) 1948 (EEG studies during CO_2 coma).
46. Wynn, V.: Carbon dioxide therapy in clinical medicine, M. J. Australia *36*:448, 1949.
47. Schaffer, K. E.; Storr, H., and Scheer, K. E.: Ueber langdauernde Einwirkung verschieden hoher CO_2 Konzentrationen auf Meerschweinchen, Arch. ges. Physiol. *251*:741–64, 1949 (Effect of prolonged exposure of guinea pigs to various CO_2 concentrations).
48. Schaffer, K. E.: Die Beeinflussung der Psyche und der Erregungsablaeufe im peripheren Nervensystem unter langdauernder Einwirkung von 3% CO_2, Arch. ges. Physiol. *251*:716–25, 1949 (Effect of prolonged sojourn in 3% CO_2 atmosphere on mentality and excitation processes in peripheral nervous system).
49. Meduna, L. J., and Gyarfas, Kalman: Motor and sensory phenomena during therapeutical carbon dioxide inhalations, Dis. Nerv. System *10*:No. 1 (Jan.) 1949.
50. Altschule, M. D., and Sulzbach, W. M.: Effect of carbon dioxide on acrocyanosis in schizophrenia, Arch. Neurol. & Psychiat. *61*:44–55 (Jan.) 1949.
51. Pollock, G. H.; Stein, S. N., and Gyarfas, K.: Central inhibitory effects of carbon dioxide. III. Man, Proc. Soc. Exper. Biol. & Med. *70*:291–292 (Feb.) 1949; Abstr. No. 4029 in Psychological Abstr. *23*:505 (Sept.) 1949.
52. Kindwall, J. A.: Carbon dioxide narcosis therapy, Am. J. Psychiat. *105*:682–685 (March) 1949. Discussion: P. H. Wilcox. Co-authors: Danziger, L.; Headlee, R.; Osgood, C. W.; Ruskin, B. A.; Spear, H. G.
53. Bain, J. A., and Klein, J. R.: Effect of carbon dioxide on brain glucose lactate, pyruvate, and phosphates, Am. J. Physiol. *158*:478–484 (Sept. 1) 1949.
54. Pollock, G. H.: Central inhibitory effects of carbon dioxide. I. Felis domesticus, J. Neurophysiol. *12*:315–324 (Sept.) 1949.
55. Meduna, L. J.: A neurophysiological theory of psychoneuroses, J. Nerv. & Ment. Dis. *110*:(Nov.) 1949.
56. Liest, L. J.: Personality mutation following carbon dioxide inhalation, Dis. Nerv. System *10*:333–338 (Nov.) 1949.
57. Wilcox, P. H.: Psychodynamic facilitation with gas anesthetics. In Chap. 31, Shock Therapy (Spiegel, E. A., ed.): Progress in Neurology and Psychiatry, Vol. 5. Grune & Stratton, New York, 1950, pp. 564–5.
58. Meduna, L. J.: Carbon Dioxide Therapy—A Neurophysiological Treatment of Nervous Disorders. Charles C Thomas, Springfield, Ill., 1950.
59. Meduna, L. J.: Clinical and biochemical indications of the convulsive and the carbon dioxide treatments, Congrès internat. de psychiat. *4*:135, 1950.
60. Sargent, W., and Slater, E.: The treatment of obsessional neurosis, Proc. Roy. Soc. Med. *43*:1007–1010, 1950.
61. Shorvon, H. J.; Rook, A. J., and Wilkinson, D. S.: Psychological treatment in skin disorders with special reference to abreactive techniques, Brit. M. J. 2:1300–1304, 1950.

62. Laine, J.: Le traitement par l'anhydride carbonique de L. J. Meduna. Encephale, *39*:523–8, 1950 (The L. J. Meduna carbonic anhydrase treatment).
63. Moussatche, H.: Acao inibidora do gas carbonico sobre as convulsoes experimentais III. Experiencias na crioepilepsia da ra. Mecanismo da acao inibidora do gas carbonico nas convulsoes, Mem. Inst. Oswaldo Cruz. Rio. *48*:219–26; English trans. 227–37, 1950.
64. Marcussen, R. M., and Wolff, H.G.: Studies on headache: 1. Effects of carbon dioxide-oxygen mixtures given during pre-headache phase of the migraine attack. 2. Further analysis of the pain mechanisms in headache, Arch. Neurol. & Psychiat. *63*:42–51 (Jan.) 1950.
65. Schaffer, K. E.; Klein, H., and Zinck, K. H.: Experimentelle Untersuchungen ueber den Zusammenhang von Mark und Rinde der Nebennieren unter langdauernder CO_2 Einwirkung, Klin. Wchnschr. *28*:179–84 (March 15) 1950 (Experimental studies on relation between adrenal medulla and cortex during prolonged exposure to CO_2).
66. Poole, C. P.: An examination of some of the aspects of carbon dioxide narcosis therapy, Presented at Southern Soc. Phio. & Psychol. April 6–8, 1950, Nashville, Tenn.
67. Wehrli, S.: Zwei toedliche Kohlendioxydevergiftungen und ihre Ursachen, Schweiz. med. Wchnschr. *80*:335–7 (April 1) 1950 (Two cases of fatal carbon dioxide poisoning and its causes).
68. Acosta, Nodal C.: Combination of narco-analysis and therapy with CO_2, Arch. Neur. Psychiat., Havana *5*:(June) 1950; Abstr., Am. J. Psychotherap. *5*:131–2 (Jan.) 1951.
69. Shor, A.: The use of CO_2 in inhalation therapy, Ohio M. J. *46*:664–5, 7–50.
70. Schaffer, K. E.: Adaptation of men and animals during prolonged exposure to increased carbon dioxide concentrations, Am. J. Physiol. *163*:(Dec.) 1950.
71. MacRae, R. I.: Carbon dioxide-oxygen inhalation treatment, J. Am. Osteopath. A. *51*:186, 1951.
72. Callaway, J. J., and McKusick, V. A.: Carbon dioxide intoxication in emphysema; emergency treatment by artificial pneumoporitoneous, New England J. Med. *245*:9–13, 1951.
73. Altschule, M. D.: Effects of factors that modify cerebral blood flow on hallucinations in schizophrenia, J. Clin. & Exper. Psychopathol. *12*:123–51.
74. Corabouef, E.: L'action particuliere du CO_2 sur le nerf myélinisé et son indépendence la l'égard du *p*H, Compt. rend. Soc. de biol., Par. *145*:544–547, 1951 (Special action of carbon dioxide on the myelinated nerve and its independence of *p*H). Abstr.: Excerp. med. *5*:831 (July) 1952.
75. Schaffer, K. E.; Cornish, E. R., Jr., and Smith, F. S.: Oxygen consumption and carbon dioxide excretion of guinea pigs under basal conditions on air and exposed for four hours to 3% CO_2 and 21% O_2. MRL Report No. 179, 10, 138–45, 1951.
76. Wilcox, P. H.: Psychodynamic facilitation with gas anesthetics. In Chap. 30, Shock Therapy (Spiegel, E. A., ed.): Progress in Neurology and Psychiatry, Vol. 6. Grune & Stratton, New York, 1951, pp. 497–9.
77. Wilcox, P. H.: Psychopenetration. Dis. Nerv. System 12:35, 1951.
78. Baars, C. W.: The pharmaco-dynamic treatment of psychoneuroses by use of carbon dioxide inhalations, Minn. Med. *34*:51–53, 1951.
79. Palmer, H.: Three aspects of ego-organization in relation to ether abreaction therapy, J. Ment. Sc. *97*:388–393, 1951.
80. Potts, F.: Tratamiento farmacologice de las neurosis con el dioxide de carbano, Arch. Neurol. & Psiquiat. *6*:5–10, 1951.
81. Milligan, W. L.: Treatment of psychoneurosis—modified carbon dioxide abreactive technique, Brit. M. J. *1*:1426–1428, 1951.
82. MacRae, L. D.: Carbon dioxide in obstetrics, Dis. Nerv. System *12*:(Jan.) 1951.
83. Stephens, W. Mary: The central nervous system changes resulting from increased concentrations of carbon dioxide, J. Neuropath. & Clin. Neurol. *1*:(Jan.) 1951.
84. Smith, H. B., and Peterson, A. L.: Carbon dioxide treatment of anxiety states, J. A. M. A. *145*:1151 (April 14) 1951.
85. Laget, P.; Vianna, U., and Lavigne, S.: Effets protecteurs de l'anhydride carbonique vis-à-vis de la dépolarisation anoxique des racines rachidiennes de mammifères, Compt. rend. Soc. de biol. *145*:629–32 (May) 1951 (Protective effects of carbon dioxide toward anoxic depolarization of spinal roots of mammals).

86. Leusen, I.: Influence of different concentrations of CO_2 and bicarbonate on the respiratory center, Arch. internat. de pharmacodyn. et de thérap. *87*:248–50 (July) 1951.
87. Schaffer, K. E.; Cornish, E. R., Jr., and Smith, F. C.: Oxygen consumption and carbon dioxide excretion of guinea pigs under basal conditions on air and exposed for four hours to 3% CO_2 and 21% O_2, Bu. M. Project No. NM 002.015.03.04 MRL Report No. 181. *10*:21 (Aug.) 1951.
88. Silver, G. A.: Carbon dioxide therapy, North Carolina M. J. *12*:(Oct.) 1951.
89. Pirsch, J. G., and McCrum, W. R.: Effect of varied CO_2 concentrations of respired air on the EEG of the cat, Proc. Soc. Exper. Biol. N. Y. *78*:430–1 (Nov.) 1951.
90. Weaver, O. M.; Peterson, D. B., and Anderson, W. H.: Carbon dioxide therapy of the psychoneuroses, Dis. Nerv. System *12*:No. 12 (Dec.) 1951.
91. Phillips, R. H.: An alcoholic and amnesic patient treated with carbon dioxide, Delaware M. J. *24*:208, 1952.
92. Freeman, T.: Comments on views underlying the use of ether and carbon dioxide in psychotherapy, Brit. J. M. Psychol. *25*:148, 1952.
93. Fay, T.: Effects of carbon dioxide (20%) and oxygen (80%) inhalations on movements and muscular hypertonus in athetoids, Tr. Am. Neurol. A. 77th meeting, 225–7, 1952.
94. Peterson, A. L.: Experience with carbon dioxide therapy in psychiatric outpatients, Arch. Neurol. & Psychiat. *67*:699, 1952.
95. Wilcox, P. H.: Psychodynamic facilitation with gas anesthetics. In Chap. 33, Shock Therapy (Spiegel, E. A., ed.): Progress in Neurology and Psychiatry, Vol. 7. Grune & Stratton, New York, 1952, pp. 562–4.
96. Therman, P., et al.: Results with carbon dioxide sensitivity tests in neurotic patients, Arch. Neurol. & Psychiat. *67*:698, 1952.
97. Kalinowsky, L. B., and Hoch, P. H.: Shock treatments and other somatic procedures in psychiatry, second ed. Grune & Stratton, New York, 1952.
98. Meduna, L. J.: The carbon dioxide treatment, Biology of Mental Health and Disease (27th Ann. Conf. of the Milbank Memorial Fund). Paul B. Hoeber, Inc., New York, 1952.
99. Lorenz, W. F.: Use of carbon dioxide in dementia praecox, Biology of Mental Health and Disease. Paul B. Hoeber, New York, 1952, chap. 34, pp. 568–72.
100. Jackman, A. I., and Schorr, C. A.: Evaluation of carbon dioxide therapy of the neuroses, J. Clin. & Exper. Psychopath. *13*:(Jan.–March) 1952.
101. Busse, E. W.; Parry, T. M.; Goldensohn, E. S.; Whitehead, R. S., and Draper, W. B.: Alteration of cerebral function in man produced by diffusion respiration and prolonged inhalation of carbon dioxide, Dis. Nerv. System *13*:(Feb.) 1952.
102. Schaffer, K. E.; Cornish, E. R., Jr.; Stuntz, S. E.; Lukas, C. A.; Brewer, H. E., and Carey, C. R.: Effect of inhalation of various carbon dioxide concentrations on the inhibitory effect of light stimuli on alpha waves and muscle potential output of the forehead, pp. 1–21, Report No. 192, Bu. Med. Project NM 002 015.03.07 (March 17) 1952.
103. Kirboe, E., and Fries, J.: Kuldioxydbehandling ved psykoneuroser a. m. Meduna. Nord. med. *47*:969–71 (July 11) 1952 (Meduna's carbon dioxide therapy of psychoneuroses).
104. Gyarfas, K., and Pollock, G. H.: The subcortical effects of carbon dioxide in the cat, Arch. int. pharmacodyn. et de thérap. *90*:233–40 (July 1) 1952.
105. Brage, D.: Carboencefaloshock; produccion del shock catalepsico por el carbogeno intrarraquideo, Sem. med., Buenos Aires *101*:10–11 (July 3) 1952 (Carbon dioxide shock therapy; production of cataleptic shock by intraspinal injection of carbon dioxide).
106. Liest, L. J.: Carbon dioxide inhalation therapy in the management of the psychoses, J. Nerv. & Ment. Dis. *116*:(August) 1952.
107. Moriarty, J. D.: Carbon dioxide inhalation therapy of the neuroses, J. Clin. & Exper. Psychopath. *13*:No. 3 (July–Sept.) 1952.
108. Margaria, R.: Sulla combinazione del CO_2 con gli aminoacidi e con l'emoglobina, Schweiz. med. Wchnschr. *82*:990–3 (Sept. 27) 1952 (Combination of carbon dioxide with amino acids and hemoglobin).
109. Bennett, A. E.: The value of the so-called shock therapies, Ann. West. Med. & Surg. *6*:No. 9 (Sept.) 1952.

110. Pelage, S.: Vichy, une nouvelle technique de nouvelles indications; la cure plutonienne; utilisation des gaz thermaux selon la technique de von Meduna, Rev. med. chir. mal. foie 27:15–7 (Oct.) 1952.
111. Pollock, G. H., and Gyarfas, K.: Synergists and antagonists of carbon dioxide in central nervous system, J. Nerv. & Ment. Dis. 116:454–5 (Nov.) 1952.
112. Arends, R. L.; Rayburn, C. M.; Draper, W. B., and Whitehead, R. W.: Effect of diffusion respiration and of inhalation of high concentrations of CO_2 on plasma volume, thiocyanate space, blood cells and O_2 capacity, Am. J. Physiol. 171:507–12 (Nov.) 1952.
113. Schuff, B.: La utilizacion del anhidrido carbonico en terapeutica por el metodo de Meduna, Sem. med., Buenos Aires 101:625–8 (Nov. 6) 1952 (Meduna method in therapeutic use of carbon dioxide).
114. Meduna, L. J., and Jackman, A. I.: Carbon dioxide inhalation therapy. Psychiatric treatment, Proc. A. Research in Nerv. & Ment. Dis. 31: Williams & Wilkins, Baltimore, 1953.
115. Silver, G. A.: Carbon dioxide, Psych. Quarterly 27:1 (Jan.) 1953, p. 52.
116. Meduna, L. J.: The mode of action of carbon dioxide treatment in human neuroses, J. Nerv. & Ment. Dis. 117:(Jan.) 1953.
117. Smith, J. A.: An evaluation of the results of treatments of 33 patients with carbon dioxide inhalations, Am. J. Psychiat. Clinical Notes 109:626 (Feb.) 1953.
118. Smith, Jackson A.: An evaluation of the results of treatment of 33 patients with carbon dioxide inhalations, Am. J. Psych. 109:No. 8 (Feb.) 1953.
119. Meduna, L. J.: A modification of carbon dioxide treatment using nitrous oxide, Dis. Nerv. System 14:No. 4 (April) 1953.
120. Silver, G. A.: Carbon dioxide therapy, Southern Med. J. 46:No. 3 (March) 1953.
121. Wilkinson, W. E.: Subcoma, coma, and convulsive carbon dioxide therapy, U. S. Armed Forces M. J. 4:No. 5 (May) 1953.
122. Moriarty, J. D.: Evaluation of carbon dioxide inhalation therapy, Presented at the meeting of the Am. Psychiat. A., Los Angeles, Calif., May 7, 1953.
123. Hargrove, E. A.; Bennett, A. E., and Steele, M.: An investigational study using carbon dioxide as an adjunct to psychotherapy in neuroses, Presented at the meeting of the Am. Psychiat. A., Los Angeles, Calif., May 7, 1953.
124. LaVerne, Albert A.: Rapid coma technique of carbon dioxide inhalation therapy, Dis. Nerv. System 14:No. 5 (May) 1953.
125. Jackman, A. I.: Carbon dioxide convulsive treatment, Dis. Nerv. System 14:No. 7 (June) 1953.
126. Liengme, A.: De la thérapeutique des psychonevroses par inhalations de CO_2, Rev. méd. de la Suisse Romande 73:No. 6 (June 25) 1953.
127. Gellhorn, E.: The physiological basis of the carbon dioxide therapy of psychoneuroses, J. Ment. Sc. 416:373 (July) 1953.
128. MacRae, L. D.: A cinematographic analysis of reactions under CO_2 treatment, Dis. Nerv. System 14:No. 7 (July) 1953.
129. LaVerne, Albert A., and Herman, Norris: Carbon dioxide inhalation therapy, Dis. Nerv. System 14:No. 7 (July) 1953.
130. Peck, Robert E.: Standardization of CO_2 treatment, Dis. Nerv. System 14:No. 8 (Aug.) 1953.
131. Smith, Anna May: Treatment of stutterers with CO_2, Dis. Nerv. System 14:No. 8 (Aug.) 1953.
132. Frank, J. A.: A critical evaluation of carbon dioxide oxygen inhalation therapy in mental disorders, Am. J. Psych. 110:No. 2 (Aug.) 1953.
133. Fay, Temple: Twenty per cent carbon dioxide inhalation in muscular rigidity, J. A. M. A. 152:(Aug. 22) 1953.
134. Meduna, L. J.: Physiological background of the carbon dioxide treatment of the neuroses, Am. J. Psychiat. 110:No. 9 (March) 1954.
135. Meduna, L. J., ed.: Symposium on carbon dioxide therapy, Dis. Nerv. System 14:1953.

The Classical Sakel Shock Treatment

A REAPPRAISAL

Manfred Sakel, M.D., Sc.D.

NEW YORK, N. Y.

Twenty-seven years have elapsed since I introduced a new psychobiological approach for a somatic physiological treatment of the whole spectrum of nervous-mental-emotional disorders.* Before briefly reviewing the history of the treatment and bringing my experience with it up to date, two observations must be made.

The first is a general proposition which is responsible for the contents of this paper: it may be said that an entirely new treatment that has survived the test of time has proved its value, despite the fact that the rationale for its effectiveness may not yet be clearly confirmed. There is as yet no explanation sufficiently substantiated by experiment of why the Borderline Insulin Treatment and the Classical Shock Treatment are effective, but the favorable results obtained over a period of 27 years of constant experience with all kinds of psychiatric problems have, in experience, established their value beyond any possibility of doubt.

In our days of flux, when there is a tendency towards blurring fine definitions and towards a ready acceptance of catch words and superficial slogans so that the hard reality of the facts can be avoided, when the terminology is mostly of a popular scientific type but the content is emotional with as much abstraction as possible, it is necessary to make an attempt to define the word *psychiatry* as clearly as our knowledge permits.

We do not know very much about the origin of man. We still know next to nothing about the substance which is generally glibly referred to as "Mind." We speak about it as a concrete object. Everyone thinks he knows what it is; yet we cannot even be sure that everyone has the same concept of it. The same thing can be said about the overused words "personality make-up" and "human behavior." Psychologists, psychiatrists, and, as we have experienced lately, even zoologists, have tried their hand at these definitions. The truth still remains that we are no nearer to understanding the why and the how of the mental, emotional, and interpersonal reactions of the mind.

The second observation is specific and explains the necessity for the existence of this paper. Despite the fact that the Borderline (subshock) Insulin Treatment and the Classical Insulin Shock Treatment have been at the disposal of the medical profession for about a quarter of a century, millions of sufferers from psychiatric illnesses have not been given the chance to benefit by them. This unhappy situation has a simple explanation which I shall endeavor to expand in the course of this paper.

---

* In the 1934 edition of *Psychiatrisch-Neurologische Wochenschrift* (no. 11) Professor Schaffer, head of the Budapest Medical School, published a reaffirmation of my discovery. It was obvious from the paper that for some time Professor Schaffer had treated many cases in his hospital with the "Sakel" method. These cases were described in detail. The first full volume book about the "Sakel insulin treatment" was published by the associate and successor of Professor Schaffer, who was Professor Ladislaus Benedik.

Because psychiatry deals with illnesses of the mental and emotional realm, which, though only perceivable by our mind and not by our senses (as in physical illnesses), are still illnesses of the organs which produce them, it cannot offer any standards of measurements whereby deviations from the normal can be listed and established. For these reasons, psychiatry had of necessity a hard start. There were and are no standards and measurements which can be strictly defined and which can convey to an observer the impression that they are expressions of normalcy or abnormalcy. These standards were indispensible in creating the modern medicine for physical illnesses.

The main prerequisites which served man in the achievement of these high goals in science are not available in psychiatry. It is therefore small wonder that in the field where no defined borders can be established and fixed, there was and is an enormous place for anyone who wishes to postulate theories. He cannot experience the inhibitions or limitations which might arise from the need for proof or disproof. His conviction is sufficient. The only quality which seems to be required, and which indeed is attractive, is brilliancy of presentation. This is, of course, human, and human beings, not having concrete scientific tools to handle, naturally resort to this method in their frustration.

This history of psychiatry abounds with theories, postulations, dogmatisms and persuasive treatments which are only rivalled in quantity by the lamentable lack of cures.

Psychiatric diseases contrary to diseases recognized as physical have the common denominator of presenting dysfunctions in the realm of mentally perceivable actions alone. They must therefore be considered as the end product of a deviation from the philogenetically imprinted pattern of the nerve cell to respond to external or internal stimuli in a way established as normal since the beginning of the development of man. These responses constitute in toto a sequence of actions which are commonly referred to as "the mind" or "emotional content."

There is great variety in the mental and emotional diseases which, as said before, are only perceived by the *mental* perceptions. The diseases can be as distinct from each other as a superficial scratch on the skin is distinct from a deadly cancer. For example, a too intense anxious reaction due to a bonafide problematical condition confronting a patient is distinct in its nature from a complete schizophrenic confusion or a paranoid logical deduction from a delusional premise.

Psychiatry must therefore be conceived as an over-all term for a complex variety of diseases as well as overcharged distress reactions to complicated situations. In the same way, Internal Medicine is the overall term for disorders extending from malnutrition in distressed areas caused by economic conditions, on the one hand, to cancer (which is not influenced by any economic or external circumstance) on the other.

This lack of distinction in connection with the causes of elusive and undefinable psychiatric manifestations has given an opportunity for speculators and formulators of spectacular postulations whose contentions could not be based on objective tests.

The supreme law of inertia, which without any doubt applies to the pattern of the mental activities of man, and the natural dislike of change which demands a contradiction of the

Natural Law enforcing the minimum expenditure of energy in the process of Life, are not confined to medicine alone.

History is full of examples that substantiate the strength of this tendency. Galileo was persecuted because he would not, with his superior mind, deny the absolutely provable fact that the earth moves round the sun and not vice versa as the scriptures stated: nor could he convert the majority to the acceptance of the real facts. From this example, it is obvious that it sometimes takes centuries to reconcile man's tendency to adhere to past convictions with newly acquired knowledge. No revolution is strong enough to supersede an existing pattern of thought and achieve an irrevocable establishment of a new one. It cannot (human nature being what it is) cause the people with position and standing to abandon their cherished ideas, however false they may be.

In order to understand the psychology of man, one should take consideration of the fact that physicians and scientists come, apart from their professional specialization, under the general psychological gravity of man. It should be recalled that not only in the supreme logical deductions of Copernicus, Galileo, and Newton, but in the field of experimental medicine, Semmelweis encountered the same law of inertia. He was unable to save millions of mothers because his superiors could not see the facts as he did. Nor should it be forgotten how difficult it was for Robert Koch to establish the factual basis of infectious diseases by visible demonstration of the cholera bacillus in the face of Metchnikoff's world-famous and profoundly accepted theory of miasma. Examples of this nature could be given ad infinitum and I have brought these few to show that not sudden revolutions (discoveries) alone but evolution is ultimately successful in forcing man to a gradual acceptance of new facts. If visible and measurable disciplines of science have been so difficult to establish in the ascent of human knowledge, one should not be discouraged by the fact that it will take a little longer to achieve the same in all aspects of human endeavor including the medical aspect which is perceivable by the mind only, that is, psychiatry. Progress is steadily being made by man in spite of reverses. The same is true in psychiatry.

Psychiatric problems can roughly be divided into two groups with two fundamentally different underlying constructions. One cause of maladjustment may be traced to the course of a particular patient's personal development, that is to say, that in his ontogenetic emotional or associative pattern, some fault or trauma deviated him from a more normal course of development. These people will be in need of psychiatric help and the cause of their difficulties can rightly be assumed to be psychological in nature. Psychiatric traumas are usually incurred in the formative stages of the *imprinting and ingraining* of the responses and attitudes of these patients. They become frustrated, deviated and may even present a picture of deeper seated really nervous dysfunctions but will have *no break* in the real phylogenetically anchored nervous introcellular pathways of responses acquired by selection in the long course of human development. This is the group to which patients belong who were badly moulded but where the characteristic of their deformation is not the outcome of a biochemical and organic dysfunction but a psychological personality distortion. Medical physiological additional help will in this case reinforce the supportive psychological treatment.

The second group definitely belongs to the realm of experimental physical medicine. Its

"abnormalcy" has its origin in entirely different mechanisms. A "break" in the phylogenetically engrained patterns and pathways of nervous responses, which normally flow in an enforced course, is the outcome of a noxa. The enforced flow of responses in these established intercellular ruts which must follow rigidly, step by step in a way similar to the constellation of the intercellular particles and electrons in a magnet, is suddenly disturbed.

The route on which the impulse should normally travel may be derailed by a disturbance in the intercellular pathways or patterns of transmission. The latter should not be thought of in neurological terms but as specific constellations of *electromagnetic primary particles* in the cell itself. These are not visible, even under a microscope, but nevertheless, they must exist. We cannot do without assuming their existence just as we cannot do without assuming electronic waves on which impulses travel. A stimulus releases an impulse on the perceiving nerve cell which is transmitted on these intercellular wave lengths, which I call intercellular pathways and patterns, to the adjoining cellular unit through the synapsis until it reaches the normal end point of perception. This impulse which is converted from a stimulus will then be forced to continue its way in an insulated pattern or pathway until it reaches its destination. Under normal conditions, this impulse will not be able to "jump" the rail nor illicit impulses, which are not originally converted from stimuli in this chain of perception or "wave-lengths", nor create in the final destination point a perception which is unrelated to the original stimulus.

If the route is derailed, completely new phenomena, not normally experienced when this chain of pattern is insulated from the others and is strictly specific, will be evident. I refer here to hallucinations, delusions, and the host of other unmotivated and uncalled for actions and reactions. This group of patients has definitely suffered a "structural" damage. As said before, this does not imply a structural damage in organic or microscopically visible implications, but a reversible damage in the biochemicoionic or possibly electronic magnetic constellations of the invisible particles in the nerve cells.

One can only visualize the process which ensures the insulation and isolation of the pathways and patterns on which impulses travel and the damage which causes them to "jump the rail." If this should happen in the intercellular pathways and patterns, and we have to assume that each specific neuronal cell has a number of abandoned and phylogenetically antiquated and inactive pathways, the stimulus converted into an impulse will travel on a nonaccustomed route. Conversely, the intercellular pathways which can be visualized as a fixed constellation of *electromagnetic particles*, may be pathologically disturbed or rearranged and may thus create a completely abnormal pathway. We can compare this with the static or metallic interference in the electromagnetic tape which produces a cacophony of a symphonic and melodic harmony.

To express this in simpler terms, it may be advisable to bring the above-said into line with hypotheses in other abstract sciences, and in particular with physics. We know more about these other sciences, but we are still dealing with and perceiving the one and only universal energy which in a mental condition is translated into thoughts and emotions, and in physics, into measurable manifestations. In the latter we deal with hypotheses which are equally intangible but which have already been proved workable and helpful. I am referring spe-

cifically to the field of electronics and the magnetic constellations in the magnetized tape of a tape recorder. Though elusive and inconcrete, the theory behind this phenomenon demonstrates its soundness. The sound produced by a voice transmitted through a series of electronic tubes is capable of changing the originally polarized *constellation of particles* which are patterned in a certain direction in the tape and will produce a high fidelity recording and reproduction of the specific sound.

It is helpful to imagine the perception of psychic phenomena released by stimuli in the same way as the sound recording is perceived on the magnetic tape. Intercellular patterns and pathways are illicited by stimuli in human beings in the same way and with the end result of a conditioned reflex in *Pavlov's* sense of the word. These intercellular pathways and patterns become fixed and stable under normal circumstances and will remain so unless there is a cataclysmic interference in the cell structure.

Schizophrenia, the gravest and most widely spread single group of real psychiatric diseases, (as opposed to functional ones) may appear in a variety of schizophrenic pictures and is the result of such a cataclysmic interference in the structure of the nerve cell.

In many schizophrenic patients, we may encounter a mirror reversal of the normal constellations of particles forming the intercellular pathways and patterns. Their reaction will appear logical but will be the exact opposite of their previous ones. The patient will hate the person he formerly loved and love the person he formerly hated. The same will frequently happen in the instinctual domain. The perfectly normal heterosexual may suddenly show a seemingly plausible performance of being a real homosexual. These cases are so common that they have given rise to the speculation in some schools of thought that paranoia, for example, is the end result of a repression of homosexual tendencies. The fact that the homosexual quality in these patients is only the most conspicuous of the other reversed or subverted emotional feelings is overlooked. All are symptoms of the basic schizophrenic primary process and disease. This can be proved without a doubt by those trained in the Classical Insulin Shock Treatment where, at a given moment in the course of the treatment, a "reversal or normalization" of the behavior of the patient can be seen for a short time. Such a patient will revert for shorter or longer moments, at a certain point during his hypoglycemia, to his previous normal personality pattern and voice distress and surprise about the feelings and drives he experienced a few moments before.

In my time as a medical student, those of us who chose to specialize in psychiatry were taught to deal with all nervous-mental-emotional diseases by employing the scholastic remedies of a psychological handling of symptoms. For lack of knowledge of a more scientific medical technique, the sicknesses themselves remained untreated. Consequently, by emulation of teachers and by force of habit, one generation of doctors after another went on thinking in terms of symptoms, mistaking them for illnesses, instead of attacking fundamental causes.

I, too, was a product of such a mental climate, and I was educated in the art of classifying, describing, and analyzing the psychological interplay and reverberations of the perceptible symptoms of insanity, psychoses, neuroses, and all other psychiatric ills, so brilliantly expounded by Freud, Adler, etc. But being inquisitive and a nonconformist by nature and

therefore prepared to admit the unsatisfactory end results of these procedures, it became increasingly evident to me that the beneficial outcome of the scholastic, psychological approach to the medical problems of psychiatry was entirely incommensurate with the widespread reputation and acceptance of these practices. I could not ignore the fact that the individual patient continued to be sick and to suffer despite these orthodox treatments.

My attempt in 1927 for a medico-scientific treatment took shape when I came to realize that a great mistake in logic must underlie the current thinking of the psychiatrists. They had apparently become so fascinated by the exploration of the psychic mechanism of their patients that their preoccupation with the psychological difficulties had blotted out their direct awareness of and concern with the actual cause of the nervous, mental, or emotional disease entities. They had obviously confused the two. To use an analogy, they were trying to correct the deficiency of the radiance of a beam of light by manipulating its refractions and reflections, when in reality its generator was failing.

Another fact became clear to me, namely, that though man does not go on thinking and feeling when he is dead, his ability to think and feel may stop while he is still alive. It seemed to me that the higher abstract functionings of man, such as thought and emotion, are undetachable by-products of the biological substratum of the life processes. In those cases of disease in which the malfunction lies in the higher neurological centers, the phenomenon of abnormal psychological reactions will appear. To remove these, the malfunction in the nerve cells from which they stem must be cured. To deal therefore with the abnormal manifestations themselves can no more produce a cure than, to return to our analogy, to use even the best set of prisms can improve the strength of a light ray if its source is impaired. The beginning of the development of a physiological treatment for psychiatric diseases was the outcome of this reasoning.

Orthodox as this approach may seem today, its introduction met with an enormous storm of protest of serious consequence and importance for future development, because it came particularly from the older, established psychiatrists. The leaders of this opposition were men of great integrity and achievement, like Professor Wagner-Jauregg, who had won the only Nobel Prize ever awarded for psychiatry, and Professor Berze, who, with Doctors Bleuler and Kraepalin, had formulated the structure of schizophrenia and cyclothemia as distinct entities. They could not view the new premise objectively and dispassionately, perhaps because it demanded a complete revolution in their thinking and procedure.

My lack of flair for literary expression aggravated the situation. I was reluctant to spend time on filling the psychiatric journals with persuasive arguments for my techniques when I could be using both time and techniques to help patients.

Moreover, I knew from my hard-won clinical experience with this treatment that these techniques, like surgical methods, could not be learned by reading, but only by a long, practical, clinical apprenticeship under the guidance of an experienced teacher and by men with keen observation and special aptitude. I did, however, publish a preliminary short report in 1928 and a minute detailed description of my methods in September, 1933, and followed them up with approximately one article a year. But the weight of cured patients, I felt, would speak more compellingly than anything I could say in favor of my methods,

I could not at that time foresee the part that the cataclysmic events of world history would play in disrupting the continuity of my work, by preventing me from imparting directly my accumulated personal experiences.

The physiological treatment in psychiatry received quite a different reception by the younger psychiatrists. They quickly adopted the new treatment and put it swiftly to use, but they were without the proper training and understanding for the vicissitudes involved in executing it. The new treatment sounded simple when reading about it—injecting a needle and terminating with sugar or a chemical or physical process which provoked seemingly similar effects. They thought that this was all they had to do to master the treatment.

Looking back over the past 27 years at the tortuous way the progress of my new treatment in psychiatry has taken and considering the basic misconceptions that have arisen, I feel it is necessary to trace the trouble to its source. The basic misconception was caused by my initial overemphasis of the convulsion, a mistake which gave rise to the false idea that the convulsion was the prime therapeutic factor in the treatment of psychiatric diseases and, in particular, of schizophrenia. I did not appraise its great asset as being a remedial factor in self-curative depressions, but erroneously considered it capable of effecting a causative cure.

I hope in the course of this paper to correct this and to establish the salient features of the Classical Sakel Insulin Shock treatment in such a way that they cannot be misconstrued, misinterpreted, or misapplied.

As far back as 1927, clinical observation, together with the theoretical assumption that major psychoses are primarily a symptom of a pathophysiological condition, and the obvious fact that psychotherapeutic treatment alone for the various denominations was insufficient, convinced me that even the best solution of a patient's personal problems cannot by itself serve as a causative treatment of a major psychosis.

Psychoses, like fever, have to be considered as the symptoms of an illness. The mind is only the highest perceptible element of the living human being. An abstract, it cannot be termed either sick or well. These adjectives can only be applied to the tangible, physical organ, the brain, which produces and distills mental and emotional reactions. If the organ functions properly, the mental and emotional reactions are normal. If it does not, its reactions are abnormal. Psychoses differ from ordinary physical symptoms only insofar as they cause a change of personality, which is utterly baffling to the normal person. Twenty-seven years ago, this conclusion was not substantiated by experience and had to be accepted as a working hypothesis only. Now it can be accepted as a scientifically established fact that major psychosis belongs to the realm of medical psychiatry.

I started my experiments with the idea that the key to combat mental disease lay in the discovery of a physiological approach to influence the center of the autonomous nervous system, the hypothalamus, which appeared to be the bridge between physiological reactions and mental manifestations. The best-known drug to accomplish this was insulin, the main hormone regulating the adrenoinsulin interplay. It was also valuable in that it could be dosaged with the greatest precision.

My supposition was that some noxious agent weakened the resiliance and the metabolism

of the nerve cells. The weakened cell then functioned inadequately and without the usual precise specificity in the swing of the reactions or in the choice of the most recently acquired intercellular pathway. It was assumed further that a reduction in the energy spending of the cell, that is in invoking a minor or greater hibernation in it, by blocking the cell off with insulin will force it to conserve functional energy and store it to be available for the reenforcement of the cell.

By repeating such procedures the nerve cell will then be restored to previous normal strength and response and will therefore be capable of resuming normal functioning, that is, become well again.

The reasoning which lay behind the original experiments led to the introduction of the "Borderline Treatment." It was based on the assumption that insulin would act as a sympaticotonal drug which would stimulate the vagus in order to counteract the temporarily overstimulated sympaticus. It would thus have a pacifying and restorative effect on the central nervous system because it regulated its metabolic functions. The overstimulation of the sympaticus seemed to be the predominant cause of the nervous malfunction expressed in addictions and in marginal psychiatric malfunctions.

I began in 1927 to use this treatment therapeutically in influencing psychopathic conditions and addictions by using borderline doses (i.e., precoma doses) of insulin, an established *convulsion-producing* vagotonic hormone. I did this only *after* experiments with animals which permitted me to ascertain both the therapeutic and the danger limits of insulinization. The success of the Borderline Treatment led me, as early as June, 1927, to intensify the effects of insulin overdosage by giving doses large enough to bring the hypoglycemia to the point of provoking severe shocks in *psychotics*.

At first I sought to prevent the development of the convulsion in the Borderline Treatment. Up to this time, the convulsion was supposed to be the predominant reaction to hypoglycemia in man as well as in animals. After numerous animal experiments, the result of the insulin shock was successfully transformed from convulsion to coma by adding barbiturates to the intravenous insulin injection.

This encouraging result with animals enabled me to proceed at once with testing the therapeutic effectiveness of the treatment on man. One modification was made. The barbiturate was administered orally before injecting the insulin. Case after case so treated demonstrated the therapeutic value of the Borderline Treatment, and after my publication about the initial work, confirmation appeared in the publications of others, among them Professor Schaffer, head of the Budapest Medical School and teacher of von Meduna. The success achieved with addicts (alcohol, morphine), psychopaths, and psychoneurotics seemed to justify the basic assumption and urged me to proceed immediately with the development of a practical method for treatment of the more serious mental diseases.

The treatments I developed varied in degree, in intensity, and in the choice of one or another shock factor. The Borderline Treatment became Phase I of the Classical Insulin Shock Treatment. Its restorative and sedative effects proved themselves conclusively in nervous tensions, no matter what the cause, and in all forms of severe psychiatric malfunctions. The degree of benefit derived depended greatly on the skilful administration of the treatment.

With the animal experiments, coma had consistently occurred when barbiturates were added to the insulin dose. With humans, this, to my surprise, was not the case and convulsions frequently occurred despite the barbiturates and other precautions. These unintended convulsions had the unexpected effect of producing a dramatic change for the better. The symptoms particularly noted were a swift general clarification of the thought processes, the improvement of interpersonal relationships, and, above all, the conspicuous elevation of the emotional level of the patient to the point of euphoria.

Since I considered schizophrenia the paramount problem in psychiatry, I began to concentrate my efforts on inducing a deliberately planned severe shock for the treatment of this disease with, at first, as many convulsions as possible. To achieve this convulsive type of shock, metrazol was added to the insulin as an intensifying convulsive element. At the same time, the barbiturates which had been used to reduce the number of convulsions in the Borderline Treatment were omitted in treating frank psychotics. It was a disappointment to find that spontaneous insulin *convulsions* did not occur as frequently as had been anticipated from the experiments with animals.

The next step seemed to be to provoke more frequent convulsions by any admissible means, chemical (metrazol and camphor) or physical, in addition to the insulin. It appeared to be definite that the insulin shock produced spontaneously but unpredictably one of two diametrically opposed metabolic shock reactions. The two abnormal physiological conditions, convulsion and coma, appeared to be of equal and great therapeutic value for the nervous disfunctions manifest in any psychotic condition. I tried to ascertain the maximum value of one or the other in any given psychiatric condition but was much hampered by the lack of data on the subject and by the restricted field in which I had to proceed with my experiments.

However, encouraged by progressive achievement, I decided to recommend my method of treatment to the medical world. My first paper, "The Therapy of Addiction," dealing with the possibility of influencing psychopathic conditions by means of a physiopsychological approach, and suggesting a pathophysiological basis for psychopathic reactions, was consistently returned to me over a period of years by the editors of leading European medical and psychiatric publications as unacceptable. Numerous experiences of this nature caused me to hesitate a considerable time before publishing the much more important report on the outcome of my experiments, "The Therapy of Major Psychosis."

It was only after continuously confirming my successful clinical experiments for a period of five years (1927–1933) with curative results and convincing myself of the undeniable efficiency of this treatment, that I finally decided to present my experimental treatment and to publish my "new method" in treating schizophrenia. I presented it in August, 1927, to the head of the Psychiatric School in Berlin and succeeded in convincing him that it would be worthwhile to explore it officially in the Medical School. Since I was under contract elsewhere, I could not accept the position which was offered to me there, and it was therefore proposed that I should share the credit for the treatment with an associate of Professor Bonhoeffer, the head of the school.

One after the other, the associates of Professor Bonhoeffer, while accepting the propo-

sition on the surface and promising cooperation, successfully pigeonholed the treatment. The result was that for five years I was compelled to treat only my own private patients on a very limited scale.

In 1933, Professor Poetzl, who had been approached with the same proposition, forcibly opened all doors of his Psychiatric Hospital of the Vienna Medical School so that I would have the opportunity to apply this treatment to all newly admitted patients and thus be able to determine its clinical therapeutic usefulness or uselessness.

After a few months' work here, I was ready on September 3, 1933, to present a paper entitled, "The New Method of Treating Schizophrenia and Acute Confusional Insanity." Herein were described experiences gathered over a period of five years of treating major psychoses, particularly schizophrenic conditions, with an elaborate method which I called "physiological shock." The new treatment was called "Shock Therapy."

In that report I suggested the adoption of a new "grand strategy" in the treating of psychosis and affective disorders. At the same time, I placed at the readers' disposal the tactical means which I had tested and developed and which would make such a strategy possible. The procedure introduced was fundamentally different from any known orthodox methods.

I proposed in this lecture to "terminate the deadlock in the treatment of major psychosis and to adopt a physiopsychological point of view in psychiatry."

In order to overcome the—at that time—skepticism and overconservatism with regard to anything new and outside the "orthodoxy" of the psychiatrists, it was necessary to present not only statistics of successful treatments but also experimentally tested, safe, and practical methods. In this way, they could accept the challenge to prove or disprove my claims.

Paraphrasing from the lecture of 1933, I said that the method offered was both complicated and difficult. The main therapeutical principle lay in the inducement of a pathophysiological condition of insulin hypoglycemia with one of two clinical manifestations, coma-hibernation or convulsion. These conditions I termed "shock."

The following three phases were outlined in this paper as the basic elements of the new method.

1. *Adaptation Phase:* The phase necessary to find the individual therapeutic dose of insulin for each patient and the special reaction type (convulsion or coma-hibernation) of the patient as well as the optimal strength of hypoglycemia determined by the length of time in which the hypoglycemia works. (Duration of hypoglycemia.)
2. *Shock Phase:* Deliberately producing convulsion or coma-hibernation—the maximum admissible intensity of hypoglycemia; provoking by other additional means a convulsion or letting the coma-hibernation develop, depending upon which type of shock should be advisable for the curative effect.
3. *Polarization Phase:* The phase in which the achieved improvement should be stabilized or, if possible, increased by administering individually varying subcoma doses for a long period of time.

These three phases "did not have to follow each other rigidly in each case treated

for a nervous disorder. They had to be altered and administered according to the temporary demands of the patient's varying condition."

In some cases Phase 2 (shock phase) might be superfluous, and a successful result could be achieved by proceeding from Phase 1 directly to Phase 3. This meant that in some cases the whole treatment could be concluded without shocks.

To counteract the expected incredulity, I cited case histories, both from existing literature and from my own experience in which there had been observed in psychotic patients accidental, severe physiological shocks, severe enough to be followed by amnesia. The sequel of these shocks was often a temporary disappearance of the psychotic symptoms under which the patient had been suffering.

I mentioned my case of a melancholic patient, who, rescued by me after an attempt to hang himself, was freed of his melancholia by the convulsions that followed the strangulation, which I had interrupted in time to save him.

I quoted another case where a disintegrating paranoic condition of 20 years' duration repeatedly disappeared during attacks of cardial asthma to such an extent that the patient spoke during the attack with insight and detachment about her psychosis.

I mentioned my case, and Jellinek's and Stransky's, reported in medical literature, of the schizophrenic who escaped from an asylum, climbed an electric high-tension mast, suffered an electric shock, fell in convulsions to the ground, and for two weeks afterwards remained free from manifest psychotic symptoms.

With these accidental shocks, I compared the severe physiological shocks deliberately planned and executed by me for therapeutic purposes. I reported cases in which I had produced shocks in the form of either convulsions or coma through the methodical administration of the convulsive drug, insulin by itself or in combination with metrazol. In these cases the psychotic condition has been eliminated by this treatment.

In my first-reported, successfully treated cases, convulsions occurred in 3 out of 4 cases. I pointed out that convulsions induced by whatever means, strangulation, asphyxia, drugs, or electricity, suppressed the psychotic symptoms in various patients and produced a remission. An ostensibly similar result was achieved through two physiological reactions as utterly different from each other as the convulsion and the coma-hibernation.

The conclusion reached was that insulin must prove a particularly effective, basic principle in the treatment of psychosis, since it was capable of inducing a therapeutic physiological condition which contained both curative principles, the convulsion and the coma-hibernation.

I could report 86 per cent successful cures in cases of schizophrenics that had not been ill for longer than a year, if they were treated by this method. Compared with anything previously achieved in this type of psychiatric disease the figures reported by me represented a tenfold, or even fifteenfold, increase of successful cures. These stark facts could not be ignored, but despite this, the new treatment, met with a stormy resistance when I delivered the lecture.

The leading psychiatrists of the time naturally belonged to the old school, and the conception of the new therapy shook that school to its foundation. Moreover, because the

treatment was complicated, the psychiatrist had to undergo a fundamental re-education and acquire totally new experience before he could administer it.

There began an agitated campaign against the Sakel treatment and its author. My position was all the more difficult because I was too young to possess the hierarchical authority usually based on the holding of a respected, vested position. It became obvious that a new scientific mental climate and school could only be built from the ground up. In 1933, thanks to the assistance of Professor Poetzl and in the face of the strongest possible opposition, I was able on my own responsibility, to start the transformation of the psychopathic observation ward of the Clinic in Vienna into a psychiatric hospital in accordance with my own conception of what such a hospital should be. I wished it to be not merely a place of transit for new mental patients on their way to an asylum, but, like any other hospital, a place where possible cures might be achieved.

An effort was to be made in every newly admitted case to reclaim the patient by having him treated by specially trained, expert physicians (not "alienist" only) and to return him home cured. The psychiatric division of the hospital was to remain a transit station for only those patients who remained unaffected by the treatment. Previously, this division had served, according to established rules, as an observation station where the patient remained from five to seven days before being transferred to an asylum. This was because no treatment, with the exception of malaria for paresis, had been employed

Before the advent of the Sakel therapy, the main aim in dealing with the problem of mental patients, who required hospitalization, was to cause them the least possible discomfort. If a medical treatment was used, it was just as an auxiliary expedient to increase the comfort of the patient. The new therapy demanded a new attitude. The prime objective now was the achievement of the cure. The comfort of the patient was secondary.

In other branches of medicine where the causes of the illness are known and a successful therapy established and understood, the primary aim was to achieve a cure by the simplest means with the least discomfort to the patient. This ideal had not been attained in psychiatry when I introduced insulin as a therapeutic agent. The cause of the sickness was not yet definitely known and therefore the way in which the therapy worked not completely understood. But in dealing with a desperate disease, e.g., schizophrenia, when a method which promises to achieve a cure presents itself, the physician is justified in using it regardless of the dangers and discomforts which it involves for the patient, as long as it promises the prospect of an increase in the chances of recovery. So it was with the new Sakel treatment.

Throughout 1934, there were published an ever-growing number of papers dealing with my findings and confirming my claims, and the opposition of the old school began to wane. Up to the year 1936, the physiopsychologic Sakel Insulin Shock Treatment of psychosis spread and improved. It was possible to maintain training centers, exchange experiences, and work together for the common purpose in order to discover new tactical possibilities without being hampered by dividing personal schisms. The results of such common work were apparent in the papers read at the International Congress of Psychiatrists which was held in Switzerland in 1937 and dedicated solely to my "new treatment" of insanity.

Some investigators searched for a chance to simplify or to explain the *modus operandi* of the various factors of the whole shock armamentarium. Others looked for the possibility of utilizing the unusual psychological and physiological knowledge newly acquired through the application of the treatment. At that time, I advocated the provocation of convulsions by adding metrazol in hypoglycemia for special cases only. Georgi, on the other hand, advised a more common use of them.[5] This demonstrated the possibility of tactical deviation within the general framework of the treatment. This had the advantage of helping to assess their value in relation to particular mental or emotional disfunctions. To advance the possibilities of psychotherapy and to explain the unique psychological manifestations during a "shock," psychologists were called upon to collaborate with psychiatry.

This steady development of the new therapy was interrupted in 1936 when I left the psychiatric hospital in Vienna and came to the United States. I wished to establish here a center similar to the one in Vienna. It was to be primarily a curing center for incipient psychosis as well as a place for training and research in all manifestations of psychiatry, and it was also to deal with the treatment of chronic psychotics, who represent the main problem in the already overcrowded insane asylums. But my efforts in this direction failed to produce the desired result, and this, in addition to my abandonment of the hospital in Vienna, resulted in successful attempts to split up the *treatment* into "new" ones, thus creating divided camps.

This tendency was encouraged by my original but later abandoned and renounced overemphasis of the effectiveness of the convulsion in the treatment of schizophrenia. At the time of my first publication in 1933, my experience with regard to the quality and stability of recovery in individual cases and how much of this could be attributed to either convulsion or coma, could not have been sufficiently mature considering the relatively small number of schizophrenic cases which I had been able to treat in the five years prior to publication. In each of the cases I had cited, I had overemphasized the sudden and spectacular improvement which followed a convulsion. Even so, I had not omitted to point out the great therapeutic importance of the coma, particularly in psychosis of a schizophrenic nature. The result of this was that the producing of the convulsion was accepted too hastily as the main aim of a therapeutic experiment in schizophrenia.

Immediately following the official publication of 1933, I was able to resume my experimental treatment on a large scale, and I soon revised my opinion about the therapeutic value of convulsion, particularly in schizophrenia. The more experience I gathered in the realm of active medicotherapeutic influencing of the various types of psychosis, the more problems revealed themselves, and the less simple the whole subject began to appear.

Firstly, it became apparent that the disappearance of psychiatric symptoms after a shock does not mean a complete cure in every case.

Secondly, it was necessary to explain why in some cases one group of symptoms of the psychosis, e.g., the mental one, was sooner and more beneficially influenced by the treatment than the group of emotional symptoms, while in other cases, a different category of symptoms was first beneficially influenced. It also had to be determined why the less improved symptoms (separated into two different groups, such as the pronounced mental on

one hand and the pronounced emotional on the other) responded favorably to respective changes (coma-hibernation or convulsion) that occurred later in the course of the treatment. This in turn gave rise to the necessity of acquiring more conclusive knowledge as to which psychotic conditions responded more favorably to convulsions and which to coma-hibernation, in order to direct these factors of the shock into co-ordinated action in each patient according to the individual requirements.

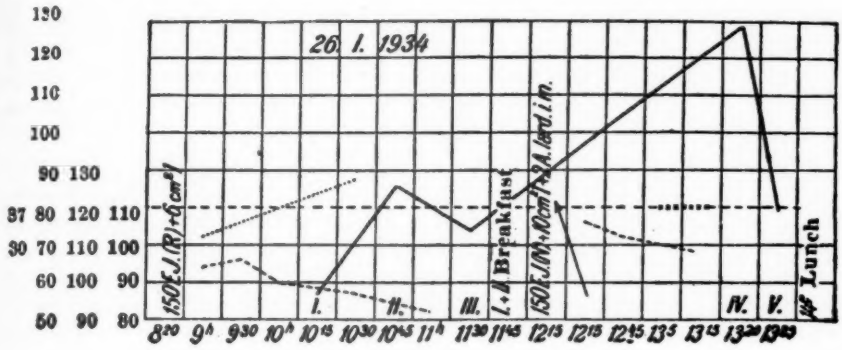
Thirdly, it was necessary to differentiate between real, i.e., basic, and symptomatic improvement. The latter often appeared real, but when closely examined showed that the patient was still not restored to his former personal makeup.

Finally, experience had to be acquired in order to discover how all these various shock possibilities, either isolated or "blended," could be utilized to increase the stability of the improvement in schizophrenics and achieve the potential restoration of their normal personalities. Only time and investigation could bring about an answer to these manifold questions. The treatment consisted of many diverse, discriminative and seemingly contradictory factors, and it was difficult in the beginning to see which was the main therapeutic factor or what factor corrected which disease condition. It was obvious that with so many unknowns, one could not with justification start to simplify the method and thus possibly lose sight of the cure. Yet this was exactly what happened.

The proposal of administering "convulsion-alone" as a therapy was enthusiastically accepted because of its simplicity. Anyone, with no expert specialized training, could apply it after a few demonstrations. After once releasing the convulsion, there was no possibility of active interference with its course. The erroneous claim to an equal efficacy of the convulsion-alone with the original Sakel insulin shock in schizophrenia led, before it could be disproved, to the rapid spreading of the spurious "short cut" and to the desertion by many of the original Sakel Insulin Shock Therapy.

Dr. Cerletti spent some time with me in Vienna in 1933 observing the Sakel treatment. He participated in the above-mentioned discussions. Five years later, he and Bini designed the electric shock machine, which produced convulsions at the touch of a push button. This was indeed simplification, since it required only a nodding acquaintance with general medicine and the physiological background of the treatment and a little training for its use. The machine very soon became standard equipment in psychiatric hospitals and sanitariums, thus isolating the convulsive factor from its true therapeutic usefulness within the context of the multifactored insulin shock therapy. The short-term symptomatic improvements resulting from the use of the convulsion-alone in cases of schizophrenia and melancholias were so dramatic that its use spread quickly. An electronarcosis method was also developed to imitate the physiological manifestations of its counterpart, the insulin coma-hibernation. This had a shorter-lived success as its uselessness became apparent sooner. Almost everyone pursued the aim of imitating the physiologically induced conditions produced by insulin by chemical or other artificial means.

As an illustration of this trend, I cite the example of von Meduna who, apparently persuaded and misled by my publications, to inject metrazol in hypoglycemia in order to provoke a timed convulsion, went on to suggest the use of metrazol alone, thus recom-



CURVE 7

1. Column: Respiration
2. Column: Temperature
3. Column: Blood sugar
4. Column: Blood pressure
5. Column: Pulse

Figure 1.

mending the convulsion produced by synthetic chemical means as a treatment by itself. His method of injecting metrazol, *intravenously*, I subsequently adopted as being more efficient than the same injections that I had been giving intramuscularly for a long period of time before him but always as an adjuvant to the insulin.

The curve in figure 1 (which appeared in the serialized articles in the *Wiener Medizinische Wochenschrift*, 1933–1934, and in my "Pharmacological Shock Treatment of Schizophrenia") indicates clearly that camphor and metrazol were used by me during the insulin-hypoglycemia to induce a convulsive type of shock long before von Meduna even claimed to have used it experimentally in animals.

In 1935, two years after I had introduced the shock treatment, von Meduna suggested as an "innovation" that convulsion should be provoked without the use of insulin as the best treatment for schizophrenia. He did not mention the fact that my treatment had been in almost universal use for several years. He conceded in the same paper that he had been influenced to substitute insulin with metrazol on the basis of the experimental findings of Doctors Stief and Tokay, which mistakenly claimed that the brain suffered less damage with metrazol than in insulin shock. Both Doctors Stief and Tokay were on the staff of the same hospital as von Meduna. The head of this hospital was Doctor Schaffer, who had already publicly supported "Sakel" insulin therapy. By the time von Meduna published his theory, I and my collaborators had already come to learn that convulsion-alone was useless and highly damaging as a therapy in schizophrenia and that it should be restricted to the treatment of emotional disorders alone.

The beneficial effect of convulsion on emotional disorders was, strangely enough, neglected at the beginning by the advocates of the convulsion-alone treatment in their desire to foster this treatment for the all-important schizophrenia. The innovation had the advantage of simplicity. A treatment, consisting of nothing but the mechanical provocation of a convulsive shock required neither special knowledge nor experience for its application.

The difference in the quality of the improvement achieved by the convulsion-alone method, even in emotional disorders, which were symptomatic only, and that achieved by the application of the Sakel insulin method could be perceived by only a few experienced physicians. The majority were not even vaguely familiar with the latter improvement which was incomparably better, because it penetrated the finer psychic regions to the point of restoring the former personality makeup. The clear evidence that was continually obtained on the inadequacy of the convulsion-alone shock in the treatment of schizophrenia was resented and ignored.

With the increase of my experience, I grew more hesitant about using forceful additional means to produce convulsion, because, as will be explained, the damaging aftereffects counterbalanced the therapeutic ones in the majority of cases. While the emotional functions of the patient were definitely beneficially affected by the convulsion, the mental ones were at best unaffected and usually definitely impaired. The result in a schizophrenic patient was that though the emotional level was lifted, the psychotic condition persisted. In the future, I left it to nature to develop the hypoglycemic shock in the direction it chose. I reserved the convulsive adjuvants for depression, melancholias, and negative stupors, where definite emotional involvement was established. Unfortunately, the fact that I had abandoned my initial overemphasis of the therapeutic value of convulsion in schizophrenia was obscured by the volume of new literature which claimed exactly the opposite. Only a very few psychiatrists took notice of the all-important revisions in this matter.

In a lecture in Paris, as early as 1935, I compared the provocation of the convulsion in schizophrenia to the use of heavy artillery in warfare. "Artillery can create a breach in the wall of a besieged city. But this does not mean that the object of the battle has been achieved. In order to complete the conquest, the city must be occupied and pacified. All branches of the besieging force have to enter it and establish there an intelligent and coordinated system of occupation which will restore the functions of the conquered area to normality."

"The cannonade of convulsion, provoked by whatever means, can destroy the defenses but cannot complete the conquest or restore normality. The restoration of normality and the reconstruction of the damaged parts are the work of the less drastic factors inherent in the insulin treatment. If it is skilfully applied, greater and longer-lasting improvement will result than that obtained through an electric or other kind of shock. These will be a restoration of the finer mental processes, a greater clarity, and smoother response in both mental and emotional spheres."

As an illustration of this, the following case is enlightening.

The patient, a lawyer, aged 30, the son of a qualified physician, was admitted to the hospital with a definite diagnosis of paranoid schizophrenia. He was treated at once with elec-

tric shock and discharged as cured exactly five weeks later. Ten days later he had to be readmitted to the same hospital where he had a second course of electric shock therapy. The slight improvement which followed was too superficial to permit his being discharged. The disorganization of his mental and emotional activities became rapidly worse. He grew destructive and inaccessible.

At the request of his parents, I took over the patient three months later. He then presented the picture of an old schizophrenic case. His behavior was manneristic, his utterances were repetitious and referred to various fractions of previous persecutions. He never completed the idea of persecutional delusion. He was strained and hesitant in his thinking, groping for thoughts and words, reminding one of an amnesic aphasia. He tried very hard to understand the questions but seldom succeeded in concentrating. His physical condition had declined. Neurologically there was a slight indication of Babinski on both sides.

Insulin treatment of the Sakel method was instituted at once. The treatment was technically difficult and did not show any effectiveness at the beginning. On the insistence of his parents, treatment was continued, and at the end of three months a slight improvement was noticeable. After this the treatment was intensified and continued in the hospital for a further six months. Following this, the parents could no longer bear the expenses, and since the patient was so greatly improved, he was tentatively discharged. The patient's improvement far exceeded expectation in that he made a quick, satisfactory adjustment to family life without the conflicts which had previously existed among members of the family. The treatment was continued for another eight months with daily visits to my office. Thus the Polarization Phase was substituted for the extension of the full treatment, which was desirable but not possible.

The extent of the improvement achieved in this case by proper application of the Classical Sakel Insulin Shock Treatment, where three previous courses of electric shock therapy had proved not only ineffective but had accelerated the process of deterioration, can be judged by the fact that the patient is still well, capable of earning his own living, and has adjusted to the community.

This brief review of the therapeutic value of the convulsion and the subsequent amnesia in schizophrenia would be incomplete without mentioning my erroneous and soon corrected opinion about the value of postconvulsive amnesia, that I set forth in the last two pages of my "Pharmacological Treatment of Schizophrenia" in 1933.

"After the patient's epileptic attack had ended, he showed the picture of a post-epileptic twilight state. As this twilight state was relieved, the patient had complete amnesia for the happenings of the past five months.... These observations suggested the tempting possibility of relieving psychosis by inducing such a severe shock that the patients would develop an amnesia complete enough to shatter both their psychosis and their psychotic behavior pattern."

This was my long-abandoned erroneous assumption in 1933, which still persists today and hampers the furthering of this potentially effective treatment. Subsequent and often identical observation taught me that amnesia cannot be a cure for the pathophysiological process underlying a psychosis. If the amnesia is severe enough to dim out the outstanding

psychotic ideas, the normal intellectual processes will suffer even more severe damage and impairment. This fact is still not generally recognized!

In the amnesia caused by all electric shocks, the level of the whole intellect is lowered, so that the outstanding psychotic ideas are not thrown into such sharp relief as they previously were. If the amnesia is less severe (the outcome of fewer convulsions), the patient, though he may lose recollections of experiences in his past life, almost never forgets the predominant pathological, schizophrenic idea for which he is being treated. The diminishing in the intensity of the psychotic idea is the counterpart of the lowering of the intellectual level and the reduced potentialities for reaction.

Retrograde amnesia, not deliberately induced, is found in only two well-known illnesses: as a consequence of a severe concussion with unconsciousness and in senile arteriosclerosis cerebri. The impairment of the retaining capacity was and is known to the neurologist in again only two illnesses; in Alsheimer's disease and in the almost-disappearing paresis.

In both these cases, the cause of the illness lies in the multiple microscopic diffused damage done to the brain matter or cells. It is therefore logical to deduce that similar conditions of brain cell damage must be at the root of each case of amnesia, however caused. The stronger the amnesia, the more severe the underlying brain cell damage must be.

To complete the clinical picture, it should be mentioned that the "slap-happiness" or "punch-drunkenness" combined with flatness, witnessed after too many "therapeutic" electroshocks remind one of clinical pictures in cases of frontal lobe tumors, or in the small group of paretics, or again in lobotomics.

The possibility of the danger of causing intellectual disturbance to the personality by repeated convulsions cannot be balanced by the brief and most insufficient improvements in schizophrenic patients, and most certainly not in manic depressives where the core of the original personality is intact. A few convulsions may help; too many can be disastrous. To substantiate this conclusion, I quote the following:

"It is evident that in a certain proportion of patients metrazol-induced and electrically-induced convulsions used in the customary therapeutic doses may produce certain disturbances in cerebral functions. As determined by changes in the electroencephalograms, those disturbances occurred in approximately 50 per cent of the patients.

"Impairment of the intellectual functions occurred much more frequently in the electrically treated patients, that is in 8 out of 13 patients. In most of these, the impairment lasted from one to several weeks. These disturbances were of the same type as those observed after metrazol, of the so-called organic type, often accompanied by an euphoric "slap-happy" state, in which the higher or intellectual functions were conspicuously affected. As in the metrazol-treated patients, impairment of the intellectual functions occurred after as few as two electrically induced convulsions, but the most marked occurred in patients who experienced more. The intellectual disturbances of the patients became increasingly conspicuous during the latter part of the course of the treatment. These observations suggest that the degree of cerebral dysfunction varies directly with the number of convulsive treatments."*

* Arch. Neurol. & Psychiat. 47:June 1942.

Moreoever: "In one case of schizophrenia, thoroughly studied with repeated electroencephalograms, the authors noted changes indicative of damage to the brain after the eleventh metrazol treatment. These changes became progressively more severe with further treatment, as did the patient's psychosis. One year later the curve was strikingly abnormal, with many three per second waves of large amplitude. In this particular case there is little doubt that the metrazol convulsion therapy played an important role in the production of the abnormal electrical activity."

The question arises whether, in view of such experiences, this method of treatment should continue to be applied. The doubt is all the greater, because the application of the classical Sakel insulin method, which may include a few spontaneous convulsions, not only has more basic and far-reaching results, but can be handled so as to produce no lasting ill effects.

The exceptional physiological condition evoked for therapeutic purposes in each insulin shock can be terminated at will by glucose, and the normal physiological condition restored without causing the slightest permanent irreversible anatomical damage. If properly conducted, no aftereffect, e.g., amnesia, or other clinical symptoms of organic brain cell damage continues beyond each individual insulin shock. Experience has shown that when used in conjunction with all the other factors at work in insulin hypoglycemia, convulsion can prove a very useful therapeutic factor in certain cases.

While I was trying to ascertain the specific therapeutic connection between the variety of therapeutic factors in the original insulin shock and ultimate success and gaining greater experience before making any further claims, many other authors, following the example of von Meduna and Cerletti, were publishing reports about their "successes." They gave figures and accounts of the number of schizophrenic patients whom they had treated with the electrically induced, metrazol-induced convulsions and whom they had discharged as cured, when in reality they had diagnosed them too hastily. They neglected to state how lasting those successes were, nor did they give a scale whereby to measure the quality of the "cures" they had achieved.

Electric convulsion-alone therapy, due to the simplicity of its application, was threatening to become a cure-all for nervous diseases, like a patent cough medicine equally effective in whooping cough and consumption. It appeared to the uninformed that there was a short cut to sanity. Psychiatry, which had suffered so long from the grave lack of an active medical therapy, thought that it had been rewarded for this involuntary waiting period by the achievement of something that no other branch of medicine could claim—a standardized and mechanical cure-all. The treatment of insanity seemed to the gullible and enthusiastic to have changed from endless hospitalization to an effortless and simple outclinic care. They became so absorbed in applying electric convulsions that they overlooked the results of them manifested in the ever-growing number of hospital patients.

But there is no short cut, neither in medicine nor anything else, and least of all in psychiatry. No one who commenced his career in scientific discipline could conceivably persist in such palpably erroneous wishful thinking. But at that time, the hope had risen so high that it was difficult to give it up even when it started to be proved fallacious.

The general application of the electroshock in psychiatry, uniform for all types of psy-

chiatric conditions, slight or grave, with the only differentiation consisting in the number of shocks, was a grievous oversimplification. It was a technological mechanization of a medical approach and a reflection of the mechanical times in which we live. No physician in another field would adopt similar, uniform methods to achieve the successful cure of an internal disease. Aware of the extent of harm which threatened the whole physiopsychological approach to the problem of insanity, particularly schizophrenia, in 1937 I decided to call attention to the danger of the schism between the whole original Sakel Insulin Shock Therapy and the "convulsion treatment." ("On the Significance of the Epileptic Convulsion as a Therapeutic Factor in the Pharmacological Shock Therapy.")

I pointed out the danger that lay in mistaking a palliative improvement for a basic one and thereby missing the advantageous moment for the effective Sakel treatment. Because of this all-important time factor, the convulsions produced by electricity alone or metrazol-alone treatment, which effects a misleading improvement, renders a great number of curable schizophrenic patients incurable. They lose the chance of being cured because of the lapse of time that has occurred since the beginning of the sickness; time during which they could have been cured but instead of which they have only been symptomatically improved, while the progress of the basic disease has continued unchecked. The Sakel Insulin Shock Treatment, in contrast to this, promises a cure and does not have the danger of a misleading temporary success.

These warnings were unfavorably received. Many physicians, who had but recently become acquainted with the new therapy, had either forgotten or had never known that it was I who had officially inaugurated the physiopsychological shock therapy in 1933; nor did they realize that it was much experience and many disappointments that had caused me later on to assign to the convulsion, as a therapeutic factor, a limited field. I considered that it should be confined to stupor in schizophrenia and depression in cyclothemia.

The appearance of many "different" therapies prevented the normal evolution of one effective approach or therapy. It also served to revive the old habit of deciding the issues connected with the treatment of insanity, not clinically at the patient's bedside, but at a desk, arguing the relative merits of those "various" and supposedly "independent" therapies. Moreover, the greater grew the number of these, the smaller became the number of practising physicians who had mastered the original Sakel Insulin Shock Therapy and who could teach it to others. Very few knew it from their own personal experience, but many could easily know the standardized so-called "independent" therapies.

Because many responsible physicians in the hospitals had, and have, no first hand up-to-date medicotherapeutic experience with the treatment, they left the practical application of the intricate medical treatment to the junior members on their staffs, who were not even qualified to appraise the new physiological approach. The result was that failures caused solely by the incompetent administration of the method were accepted as proof that the therapy itself was unsatisfactory.

I will quote Dr. Ross in order to illustrate some of the features of the trend I have just described. The following excerpts are taken from his *Pharmacological Shock Treatment of*

Schizophrenia, which he composed in collaboration with I. Murray Rossman, Wm. B. Cline, Jr., Oscar Schoerer, and Benjamin Malzberg.

"Some of the institutions discontinued insulin treatment and have limited themselves to metrazol. . . ." [i.e., convulsion by means other than insulin.]

"It was not so long ago that it was insisted in some quarters that a recovery (from schizophrenia) never occurred. If it did, the diagnosis was automatically changed. Later there was a willingness to concede that cures sometimes did take place, but the consensus of opinion was that it was a chronic, progressive disease, leading frequently and at times rather rapidly, to deterioration. In New York State, the recovery rate was given as 3.5 per cent. But as soon as the Sakel Pharmacological Shock Treatment was introduced, numerous reports of spontaneous recoveries or remissions began to appear. In some the rate was as high as 50 per cent or more. Such claims can hardly be accepted in view of the increasingly large number of dementia praecox patients that fill our mental institutions to overflowing and therefore, do not require comment. . . ."

"The shift to metrazol [convulsive treatment] seems hardly justified in the face of the figures we are submitting today. . . . It will be observed that the recovery rate for hypoglycemia treatment [Sakel method] exceeds that of the metrazol group by a ratio of 6.9 to 1.1; the rate of much improved by 2.7 to 1. Of the [Sakel] insulin group 63 per cent showed some degree of improvement, while in the metrazol group only 36 per cent were improved. Clearly the results following insulin treatment far exceeded those obtained by metrazol. Furthermore it will be observed that the recovery rate following treatment with metrazol was *less than half that obtained with the control group*, and the rate of the much improved was also higher in the control group."

To sum up, the negative results of these mass experiments are confined to the damage done to schizophrenics and the undeniable aggravation of their psychiatric condition. The positive results consist of the fact that these experiments have produced a bulk of knowledge on the value, limitations, and therapeutic specificity of the convulsion, when used in cases of depression and melancholia, and they have demonstrated the damaging effect of the indiscriminate use of the convulsion, particularly that provoked by electricity. Thus, these experiments have a scientific value which in some way compensates for the arrested progress of the wider application of the original Sakel Insulin Shock Treatment.

In order to remedy this situation for which there is no justification, there must be a better utilization of the original Sakel Insulin Shock Treatment. Its efficacy has already been proved in schizophrenia and in its application to lesser mental and nervous malfunctions. I have attempted to give the reasons for the almost incredible fact that we are not taking full advantage of the possibility of the general use of this treatment and the remaining ones are given in the succeeding pages.

The routine treatment of schizophrenia permits us to expect the recovery, within a period of five years, of only 3 per cent of the cases. In other words, if the original Sakel Insulin Shock Therapy is not applied, only 3 out of every hundred of the thousands of young persons brought yearly to the insane asylums usually recover in the following five

TABLE I

Group A—1936 to 1938

Of 82 cases 44% were recovered or much improved at the end of treatment.
Of 64 cases 31% were recovered or much improved at the end of 3 years.
Of 45 cases 42% were recovered or much improved at the end of 4 years.
Of 24 cases 33% were recovered or much improved at the end of 5 years.

Group B—1939 to 1942

Of 106 cases 63% were recovered or much improved at the end of treatment.
Of 84 cases 47% were recovered or much improved at the end of 6 months.
Of 67 cases 54% were recovered or much improved at the end of 1 year.
Of 45 cases 42% were recovered or much improved at the end of 2 years.

years. The remaining 97 cases remain in mental hospitals for the rest of their lives. Such conditions are no longer justifiable.

In the year 1933, I reported the discharge from the hospital, as successfully cured with my method of treatment, 86 per cent of all new cases. Ten years later, I could still report the same or an even higher percentage of cures. The following statistics, compiled by trustworthy authors, show the waste and failure caused by the faulty application of the Sakel Insulin Shock Therapy. I will compare my own figures of successfully completed treatments with two exceptionally instructive sets of statistical data. One of them is based on the records of Dr. Bond of the Pennsylvania Institute; the other on the material of the State Hospitals System of New York State. To quote Dr. Bond:

"Because of the variations in the attitudes which enter into the diagnosis of schizophrenia and the establishing of the condition upon discharge and later, we are sure that the results of the Sakel Insulin Shock Treatment in one hospital cannot be compared to the ordinary recovery rate in another. For this reason we keep all our comparisons within the Pennsylvania Hospital where standards have not varied as far as senior physicians can tell.

"Before the advent of shock therapy the recovery rate in schizophrenia was below 10 per cent on discharge from hospital; this rate rose in succeeding years but always remained under 20 per cent.

"Last year we separated out cases treated in 1935, 1937, and 1938 when procedures were tentative, mild, insulin dosage [not the Sakel method] held low and when the management of the unit was in the hands of one physician. Insulin dosage [nearer to the Sakel method] was kept high to increase stupor."

These cases form group B in table I. The results are contrasted in table I.

It is evident that the success of the Sakel Insulin Shock Treatment depends in a large measure upon the training, ability, and devotion of the physician who administers it. Doctor Poetzl, who wrote the preface to my *Pharmacological Treatment of Schizophrenia* in 1933, foresaw this, and I quote him to illustrate my point:

"The main difficulty involved in the general adoption of this method of treatment lies in the fact that it is difficult to learn. Any method of this sort has to be teachable and has

to be practised at the proper centers. The difficulty in learning it, however, is due to the fact that considerable experience must be acquired before one learns how far and how deep the reaction to its shock may or must be permitted to go in order to achieve the desired results."

Table II compiled by Dr. Ross will confirm this. (It appeared in the American Journal of Psychiatry, Vol. 96, No. 2, Sept. 1939.)

Table II shows a big difference in the percentages of successful treatments in the various hospitals. That difference is far too great to be accounted for by any conceivable source of error. Table II, which covers the New York state hospitals, gives us the results obtained by physicians who had been trained by me in a short elementary course of only six weeks in the application of my new method, at the Harlem Valley State Hospital in 1936. A year is the minimum time necessary to acquaint one with the treatment, and it requires much more than a year to become an expert with it.

Successful results, achieved by my students in various hospitals, ranged from 2 per cent to 37.1 per cent. Not one—not even the most successful of the contributors—attained the percentages of successful and fully authenticated cures that I had achieved. These sta-

TABLE II

Per cent Distribution of Outcome of Treatment of Dementia Praecox Patients in The New York Civil State Hospitals

State Hospital	Re- covered	Much Impr.	Im- proved	Unim- proved	Died	Re- covered	Much Impr.	Im- proved	Unim- proved	Still in Hosp.	Died
Binghampton	22.1	33.8	16.2	27.9	—	2.0	18.4	6.1	8.2	61.2	4.1
Brooklyn	21.6	28.1	28.4	21.0	0.9	5.6	16.9	8.5	2.3	56.5	10.2
Buffalo	6.0	31.9	31.9	30.2	—	9.0	17.9	4.5	3.0	62.7	3.0
Central Islip	3.0	28.6	19.6	46.4	2.4	—	15.8	7.9	2.6	71.1	2.6
Creedmoor	13.2	28.9	22.4	34.2	1.3	2.6	5.3	2.6	—	84.2	5.3
Gowanda	37.1	31.4	17.1	8.6	5.7	12.5	5.1	—	12.5	68.8	3.1
Harlem Valley	14.2	32.3	34.6	18.9	—	4.3	5.3	3.2	5.3	79.8	2.1
Hudson River	2.0	6.0	24.0	65.0	3.0	1.3	8.0	8.0	10.7	64.0	8.0
Kings Park	2.4	27.6	22.0	47.2	0.8	1.8	12.3	7.0	7.0	71.9	—
Manhattan	—	17.8	33.3	42.2	6.7	—	—	20.0	—	76.0	4.0
Marcy	2.9	55.3	26.5	33.8	1.5	—	32.0	4.0	4.0	60.0	—
Middletown	4.0	24.0	16.0	56.0	—	—	11.1	11.1	—	66.7	11.1
Pilgrim	—	20.3	31.1	47.3	1.4	2.6	7.9	13.2	2.6	65.8	7.9
Psychiatr. Inst.	22.0	17.6	16.5	44.0	—	3.2	4.8	11.3	56.5	24.2	—
Rochester	—	31.8	38.8	29.4	—	—	10.4	8.3	2.1	77.1	2.1
Rockland	—	28.6	28.6	42.9	—	2.1	12.8	17.0	—	63.8	4.3
St. Lawrence	7.0	28.1	22.8	42.1	—	—	2.1	—	10.4	83.3	4.2
Utica	29.4	17.6	20.6	30.9	1.5	9.1	6.1	12.1	3.0	69.7	—
Willard	8.6	25.9	29.3	36.2	—	3.3	6.7	—	3.3	80.0	6.7
Total	11.1	26.5	26.0	35.2	1.1	3.5	11.2	7.4	7.5	65.8	4.6
	INSULIN TREATED PATIENTS					CONTROL GROUP					

tistics clearly prove that the success or failure of the treatment depends on the ability and amount of training received by the physician in question. The treatment is like a surgical operation, which may be performed well or badly. As in surgery, the application of its procedure must be specially adjusted to every individual case, lest it result in failure. Such a failure, incidentally, differs from the failure of a surgical operation only by not being immediately apparent. The patient does not die. The failure manifests itself only in the persistence of the psychosis. When a supposedly incurable patient fails to recover after a given treatment, it is natural and human for the physician to ascribe that failure to the ineffectiveness of the treatment itself, rather than to his own inadequate use of it.

It is not fair to the patient for a hospital to abandon the Sakel Insulin Treatment because of such false conclusions and in complete disregard of the successful experiences of physicians in other hospitals. To deprive hundreds of sick persons and their families of the benefits of a possible cure is to defeat the very purpose of medicine. Yet precisely this is happening. Failures, for which the incompetent application of the Sakel Insulin Treatment alone is responsible, have created a prejudice against the treatment itself and have caused it to be almost abandoned.

It seems necessary to explain why I am inserting statistics that are not recent. It was said and will be said again by those whose mental attitude did not change that now in 1954 a new crop of literature will not necessarily confirm and justify my bringing the old statistics. To answer such criticism which appears to be superficially valid I will quote one sentence of a paper by Doctors David Landau and William Halt from *The Journal of Nervous and Mental Disease* (Vol. 118, No. 1, July 1953) as a case in point. In their article which appraises clinically electrically created ersatz conditions to imitate the physiological main factors of the "Sakel Shock Therapy," they start their paper as follows: "Deep insulin coma therapy of schizophrenia is today perhaps the *best* known and *least* used remedy for this most disabling mental disorder: this is not because some better remedy has won acceptance. . . . The objections or obstacles to the use of insulin coma therapy lie in its high cost in time of nurses and physicians and supplies." This is a very true and revealing statement of the present day handling of psychiatric cases.

It is startling in our day and age, when the smallest provincial hospital can't get a license without proving that it has sufficiently and adequately trained surgeons to perform lifesaving operations that recognized physicians will write and accept the above statement without realizing the anachronistic implication accepted in psychiatry alone. No high cost or lack of trained personnel would permit the use of ineffective icebag applications, alleviating as they may be, instead of a lifesaving operation. This fact is accepted in every other branch of medicine. But in psychiatry we became so acclimatised to neglect and false economic savings that people do not stumble upon and find most objectionable a situation where patients in a hospital are not cured by the "best known and only available treatment" because of cost and lack of specifically trained physicians. In view of such a generally spread situation it is no wonder that no competent literature about the "Sakel Shock Treatment" exists on which one could draw. One has to go back very much further for demonstration of real progressive development to find objective and reliable statistics compiled

by people who at that time took up medical psychiatry seriously and did not yet retire again to their armchair writings based exclusively on recent literature but not on their own clinical experience.

To demonstrate this I would like to mention briefly another case. One of the many letters directed to me from the physician apparently in charge of the Sakel Treatment of a hospital that claims to be one of the best in the world. This letter is as recent as August, 1954. Of course, I can not release the content of the letter, not having the permission to do so, but I will paraphrase the content. The physician in question asked me if it is correct to permit patients to drink water freely during the "Sakel Treatment"—a statement which he had read somewhere. A very well-meant, honest letter, where the physician wanted to get as much information as he could.

I mention this instance in order to demonstrate the importance and absolute necessity for the therapist to be familiar with the basic physiological happenings during the treatment in order to be able to determine clearly the more desirable therapeutic factor, that is, the convulsion or coma hybernation. If a convulsion or dry shock seems more desirable it is preferable not to permit the patient to drink water before termination. It is palpably better to keep the patient "dry." If, on the other hand, a wet shock, that is a coma-hybernation, appears to be more therapeutically helpful, it goes without saying that in such a case the patient should and must be *permitted* to drink plain water as much as he wishes before termination of his hypoglycemia. This would keep the patient "wet," increasing the perspiration and possibly facilitate the development of a coma-hybernation instead of a convulsion.

These two instances throw a glaring light on the paucity of sources available to eager physicians who would like to acquaint themselves and be trained in the intricate and correct execution of the "Sakel Treatment." In their honest attempt to treat with the only effective treatment they became aware of the fact that their knowledge of literature about it alone does not equip them at all to do so. This situation exists not only in the United States, where the long awaited and finally arrived therapy for schizophrenia has no place and is not taught in the medical schools and hospitals. At best it is mentioned in the literature. The outcome, of course, is the overcrowding of mental institutions, increasing budgets to build and maintain them, and further literary demand for more and "learned" physicians to deal with mental sickness.

It may be said, however, that recent statistics appearing here and in England indicate that doctors are again resorting to the original treatment, particularly for schizophrenia, in the capacity in which they are able. They can no longer overlook the manifest failure of the convulsion in schizophrenia and the curative results of the Sakel Insulin Treatment.

The derouting of scientific development in psychiatry was caused by my reported successes presented in my 1936 lecture on the new Insulin Shock Therapy. It aroused a great zeal among psychiatrists to participate in the newly initiated active therapy of major psychosis. Difficulties in retraining and the time involved in learning this approach, as well as the need to acquire considerable pertinent experience, prevented most of them, unfortunately, from pursuing with equal zeal the goal of equipping themselves with the requisite

qualifications for applying the intricate new treatment. It was natural for many to succumb to the temptation of accepting an oversimplification or ersatz modification of the original treatment which did not require any special re-education or learning and could be mastered by watching one demonstration, e.g., the provocation of a convulsion by an electric machine. This is the only reason that the tendency still prevails, though it is declining, towards the use of the electric shock as a therapeutic procedure in schizophrenia in the face of the steadily accumulating experience, which points to the inescapable conclusion that it is completely useless in this particular sickness. The fact has been obscured that this disease can still be treated successfully by the laborious, but effective, original Sakel Insulin Shock Therapy.

The spread of this trend can be gauged from the reports of recognized state hospitals on the basis of the statistics compiled by the Assistant Surgeon General, Dr. Kolb, who has stated:

"Insulin Shock was introduced in 1933, followed by metrazol two years later. After a lag of about a year, both were taken up with considerable enthusiasm. Insulin reached its peak in 1938 when its use was reported by 54 per cent of responding mental institutions; metrazol reached a peak in 1939, when 65 per cent of responding mental hospitals reported its use. Electric shock therapy first came into appreciable use in 1939 and was adopted more rapidly than either insulin or metrazol.

"Personnel and financial considerations rather than merit alone sometimes determined the discontinuance or decreasing use of one or all types of shock therapy.

"Convulsive shock (metrazol and electric) is more effective in affective disorders; insulin shock is best in schizophrenia."*

Dr. Ross stated in a follow-up: ". . . Of these 1,039 insulin treated patients, 134 or 12.9 per cent were considered recovered after the completion of the treatment; 282, or 27.1 per cent, were much improved and 263 or 25.3 per cent were improved. Those showing some degree of improvement thus totalled 679, or 65.4 per cent. These results are compared with the outcome of treatment among a group of 1,039 first admissions to the New York civil state hospitals who did not receive any form of shock therapy.

"In the control group 3.5 per cent were discharged as recovered; 11.2 per cent as much improved and 7.4 per cent as improved. Some degree of improvement was thus shown in 22.1 per cent of the controls as compared with 65.4 per cent of the insulin treated patients. We note especially that the latter group had a recovery rate of 12.9 per cent as compared to 3.5 per cent for the controls. Since the insulin group included a large proportion of chronic cases, whereas the controls consisted entirely of first admissions, the contrast in favor of the former group takes on a still greater significance.

"It appears, therefore, that though some patients showed various degrees of relapse in their mental status following the termination of insulin therapy, an appreciable total con-

* American Journal of Psychiatry, Vol. 99, July 1942, p. 91.

tinued to improve, a phenomenon also noted by Dr. Sakel who likened it to a process of ripening. . . ."*

He states further: "The recovery and improvement rate in the cases of insulin treated cases is significantly in excess of the rate of the control group.

"Metrazol, on the other hand, produced even fewer recovered cases than found in cases not treated by any shock therapy.

"The number of recovered cases as well as the total number showing some degree of improvement was about three times that in a control group receiving the usual institutional treatment. When cases of relatively short duration were considered, the contrast in favor of the 'treated' group was even more favorable.

"We now find that 132 patients, or 12.7 per cent, of the original total were considered recovered; 148, or 14.2 per cent, were much improved; and 192, or 18.5 per cent, were improved. A total of 472, or 45.4 per cent, were consequently either recovered or improved approximately two years after the termination of the treatment. The recovery rate remained practically constant at 13 per cent."†

An explanation of the failure of the Sakel Insulin Shock Treatment in many hospitals may be illustrated by the situation described in the excerpts from the following letter, which was addressed to me:

". . . As I have already mentioned, the lack of proper training of the physician in charge is a tremendous handicap to the efficiency of the insulin unit. In the case in question, the physician had been working for many years in a service for chronic patients; suddenly he was thrust into insulin therapy. There was no satisfactory training available other than to watch the outgoing predecessor for about a month. Some of the predecessor's views are different from yours and, as the location here is somewhat remote from the centers of learning, the new man had to rely entirely on textbooks. He soon found out that there was no science in handling the insulin shock; it is, rather, a personal art. The textbooks differ on the important points and each author advances his own view, based on his own experience and interpretation. There seems to be a tendency for anyone who treats patients to set himself up as an authority. The resulting confusion is immediately apparent to the newcomer. I believe that any organization which has the means to run a system of hospitals should also have the means to give its physicians special training under recognized authorities prior to assigning them to such work."

It must be said here that in no other branch of medicine would even the best-educated physician be expected to apply and successfully administer a new and singular treatment without acquiring adequate training. Nobody would expect a successful psychoanalytical cure on the part of a psychoanalyst, who did not have at least two years of theoretical and practical schooling, despite the fact that psychoanalysis is, in contrast to the experimental shock therapy, a psychological approach, and, therefore, both the theory and the practical application of it can be learned from the voluminous literature on the subject.

---

* American Journal of Psychiatry, Vol. 96, Sept. 1939.

† American Journal of Psychiatry, Vol. 97, March 1941.

In a treatment as complicated as the Insulin Shock Treatment, we never enquire where and how long the various authors, who are reporting success or failure, were trained and what their qualifications for administering this physiopsychological Insulin Shock Treatment are. Yet, this treatment requires not only an accomplished psychiatric and physiological knowledge, but also thorough, specialized training and experience.

Both the psychological and the physiological aspects of the insulin treatment are important, because the physiological reaction during the treatment may be different in each individual. They can also be different in the same person at various times.

The ultimate mental therapeutic result of an artificial pathophysiological process, as the hypoglycemia is, depends upon a whole series of interlocking neurohormonal and enzymic (electrical) factors mutually affecting each other, as well as upon their psychological equivalent.

The proper timing of the termination of the hypoglycemia is the most crucial point of a successful treatment. The whole course of the cure may depend upon this. This is the stumbling block where the most consequential mistakes are made—and most physicians are inclined to make mistakes if experience has not made clear to them the importance of proper timing. The important decision is often left to the assistants or is made according to routine with a preconceived standardized time limit.

The convulsive type of shock, on the other hand, is short, uniform, and explosive and cannot, therefore, be influenced, directed, or terminated by the physician after it has been released. It has to take its course. Because of these facts, the physician is more nearly ready to attend the whole process of convulsion because of the shortness of time involved (one minute) and is less likely to delegate his job to an assistant.

It required years of experience and careful observation of previously unknown reactions for me to develop my method and to learn its adjustment for individual cases. It was only after five years of such work that I published the method. I emphasized then that it could only be regarded as a general outline and that only after much experience could one deviate from this outline in order to adjust it to a given case. Better results could have been achieved had this advice been followed. The success of the reported results stands approximately in direct ratio to the duration of the physician's training and aptitude.

Reports from some hospitals obscured this picture at the beginning. The number of spontaneous insulin convulsions—i.e., dry shocks, occurring in hypoglycemia without addition of metrazol—reported by them was far greater than experience allowed one to expect. The dramatic effect of convulsion in depressed or stuporous patients was missing from their reports.

While visiting one such hospital, I discovered that the practice was to terminate a shock as soon as the slightest quiver or a light, myoclonic spasm ensued in the hypoglycemic patient. Terminating the shock in this way, though it eliminates the possibility of danger, may cause a loss of the chance to cure a patient. With sufficient experience both goals can be gained; avoiding the danger and achieving the cure.

Doctor Bond's Table II enables me to draw attention to an even more important problem, that of relapses. Naturally, not every successful cure proves permanent, but in my

experience relapses have occurred most frequently in cases which upon completion of the treatment have been considered not fully cured, but only improved.

Incorrectly and incompetently treated cases of schizophrenia, among them those treated with the so-called "convulsion treatments," showed an appreciably greater potentiality of relapse. This is true even of cases which at first show more rapid improvement. Unfortunately, this is often achieved at the cost of a fundamental and therefore more permanent cure.

To quote Dr. Ross: "Faulty treatment, proved in the long run worse than the lack of any treatment. . . . Metrazol (convulsions induced by metrazol or electricity) produced even fewer recovered cases than found in cases not treated by any shock therapy."

The price we pay for neglecting these facts is indicated by the following figures. According to Dr. Ross, the average percentage of successful cures through insulin shock in the New York state hospital system is 12 per cent. This figure is obtained from the statistics of 19 state hospitals which respectively report success in 2 per cent of the treated cases in the least successful institutions ascending to 37 per cent in the most successful ones.

There still remains the desirable and possible goal of achieving a percentage of cures which approaches that published by me in my earlier papers and which I still obtain in my private practice. This, in cases of early schizophrenia, is as high as 86 per cent and often higher, as I have already indicated.

The number of successful cures could therefore be three times as large. Moreover, even if the insulin shock treatment would do no more than accelerate the recovery in those cases which tend towards a spontaneous remission, this recovery would occur after an average of three months treatment, instead of after years of custodial care. Even for patients who ultimately suffer a relapse, the treatment would be of benefit because it would enable them to enjoy sanity for longer periods of their lifetime.

The possibility of relapse does not justify the abandonment of a helpful treatment in medicine. Why should it in psychiatry? To prolong a person's life, even for a short period, or to make it more bearable is regarded as an important aim in any other incurable disease. The patient himself reasons likewise. To prolong "mental" life and shorten "mental" death is just as important, particularly if a man in the prime of life has been struck by the disease.

Why is it that the possible utilization of a successful medical treatment to advance the problem of the insane is given so little care and attention by both practicing physicians and the responsible authorities, despite the fact that we live in an age of strong social consciousness? One reason is that the insane are deprived by the nature of their illness of the faculty to plead their cause themselves. They are in no position to awaken the community to the urgency of their plight, nor can they assist their own cause financially. Other causes, however, can be found. To analyse these, the history of psychiatry must be considered and, secondly, the obstacles which confronted the original Sakel Insulin Shock Therapy from its inception and some of which still hinder it today.

By the end of the last century and the beginning of the present one, we had succeeded in ascertaining the pathological, anatomical, and physiological basis of most illnesses. It was possible to establish, on the basis of definite knowledge, the kind of surgical operation

or chemical treatment that was capable of curing a given disease. Once the facts of the illness had been ascertained, the treatment had one purpose only, namely, the elimination of the pathogenic cause and the consequent recovery of the patient and not merely his symptmatic improvement.

Psychiatry alone was forced to pursue a different course. All attempts including Freud's to discover the pathogenic conditions of the various major psychoses had failed, except in such psychiatric conditions which were assumed to be caused by psychological factors (hysteria, neurosis, anxiety, etc.). Every effort at achieving a cure or actively influencing the course of a psychosis had proved futile.

Thwarted in this direction, the psychiatrist became increasingly preoccupied with the inner psychological content of the major psychosis in addition to the minor ones. At his desk he studied the patient's confused train of thoughts and sought to discover in them a psychological motivation for the illness. The cause of the underlying malfunction of the brain remained undiscernible.

In an illness, which lasts a long time and whose successive stages glide into one another, it is difficult to connect every individual symptom with an underlying physiological malfunction. The result was that the continuity of the basic process, in all its transitory forms, escaped observation.

In addition, psychiatrists became divided into two groups. One handled the patient at the beginning of the illness when a semblance of normal psychological contact still remained. The other observed the illness at a later phase when the patient had been transferred to an asylum. This latter group regarded the patients as "end states" (mental cripples), and the care of them was limited to the improvement of their mode of existence.

As time went on, psychiatry lagged more and more behind the other branches of medicine in the effort to achieve a cure through the removal of the pathogenic cause. Unlike other medical literature prior to the Insulin Shock Therapy era, psychiatric publications did not reflect the urgency of the basic medical problem of psychiatry, that is, the pathophysiology of psychosis. Ultimately, as the gulf between psychiatry and empiric medicine grew greater, the psychiatrist ceased to understand the physician, and the physician could know little or nothing about psychiatry.

The treatment of mental patients developed into a stereotyped routine, since an approach to a causative treatment was unknown. That routine therapy was handed down from generation to generation with some technical or doctrinal improvements but few fundamental changes. The struggle between the psychiatrist and the cause of the psychosis led to a sort of impasse, which, with time, came to be mistaken for the termination of the struggle. Some even attempted to make it look like a successful termination.

According to the prevalent attitude, a mental patient was not considered as a medico-clinical unit. The attention of the physician was focused more on the patient's personal psychological problems, warped by his illness, and the medicophysiological basis of the illness was gradually lost sight of.

The solution of a patient's psychological difficulties was, and still is, desirable. In an illness which manifests itself chiefly in the mental realm, psychological problems and mental

burdens, whether real or imaginary, cannot but be damaging. They must therefore be dealt with adequately. Psychotherapy should not lose its importance in the new physiological approach. On the contrary, its beneficial possibilities could be more fully utilized in cases which were utterly inaccessible to it before.

I have had 27 years of personal experience since I conceived an apparently successful treatment for insanity and for minor psychiatric problems. Even if the Sakel Insulin Method should not remain the final answer to the problem of mental disease, it has proved itself up to now the most valuable tool for a successful physiopsychological approach to the problem of mental disease. The fact that this treatment has survived over the period of these years and is still in successful use is ample proof that it is not the disappointment which many predicted that it would turn out to be.

The method, as generally and currently used, is either not properly administered or not fully utilized. The outcome is that its beneficial results in schizophrenia are far below what we could reasonably expect if the treatment were applied as it should be. It would be an immeasurable loss if the medical profession or society allowed the original Sakel Insulin Shock Treatment to fall into disuse for no better reason than its complex application and a combination of adverse circumstances that can be overcome.

There is a danger that the postwar period will continue the process which has been undermining the treatment for the simple reason that circumstances or lack of a basis for appreciation will hinder this discovery from being imparted to the new generation of doctors.

The institutions which use the treatment well and successfully are few and unfortunately not "vocal," that is to say, they have no influence in hierarchical places. The younger physicians, though aware of the great need of modern psychiatric training, are attracted to centers that are well-known and influential but which do not necessarily teach the most effective treatments. Such a situation may not be tolerated any longer if the problem of mental invalids is to be seriously tackled. A treatment which has already proved so promising and which contains so many possibilities for further development must not be lost.

The years of my experience have given me a clear idea of the conditions which are needed in order to obtain the best results from the Classical Insulin Shock Therapy. I therefore feel justified in proposing the following measures:

1. The steady increase of the number of chronic invalids must be checked through adequate treatment which will prevent the patient from becoming chronic. This is the only meaning that preventive treatment in psychiatry can have today, since we do not yet know the cause of the diseases and cannot therefore prevent them before they have started.
2. The special method of curing chronic cases, which was announced by me in 1937, but which, because of adverse circumstances, has not advanced to the point where it could be offered for general use, must be developed to that point.
3. There must be created a center of teaching for the proper administration of the original Sakel Shock Therapy to which physicians would be attracted in large numbers.
4. The public must be re-educated to regard mental diseases as curable if apprehended

and treated at the earliest time. It must be taught to bring every mental case in its initial state for medicopsychiatric treatment, just as is being done with regard to surgical cases, such as cancer, in order not to lose the most opportune time for achieving a cure.

5. A preventive hospital must be established for a medical-physio-psychiatric treatment of incipient mental cases. This means that new cases must be brought to a psychiatric hospital not merely for observation and then transference to an insane asylum, but for an effective medical treatment not just a symptomatic ameliorative one like the electric shock treatment.

Solely for the purpose of correcting frequently heard misinterpretations of my attitude towards the other psychiatric techniques, I state the following: the fact that I recommend the psychophysiological causative therapy for the treatment of the majority of psychiatric cases, particularly the insane, must in no way lead to the erroneous conclusion that I overlook the importance of modern psychotherapy and occupational therapy. The only reason that I apparently do not give them enough attention in this paper is that I consider them so fully established as to make a discussion of them superfluous. My attitude toward them can be illustrated with reference to the surgeon who, while discussing an operation on the stomach, could conceivably omit a discussion of the diet for the simple reason that it is taken for granted.

Psychotherapy and occupational therapy, the curative and the protective "diets" of the psyche, occupy the same position in a mental disease as the nutrition diet occupies in an abdominal operation. They are not causative therapies with regard to the more serious patho-physio-psychological processes, but by excluding damaging psychological problems they enhance curative tendencies and prevent aggravations.

There ought to exist a curative, i.e., preventive hospital in addition to and in advance of the already existing state hospitals. The receiving centers, which serve chiefly as places of observation, diagnosis, and transit, should be instructed to send new cases not just to any hospital, but to a "preventive" one. In this way, the majority of incipient mental invalids could be prevented from becoming chronic cases. Only cases which failed to respond to this treatment after a period of three to four months would then be transferred to the other mental hospitals.

The advantages of such hospitals are obvious. The recovery of the patient would be the main object while problems of management would be of secondary importance. Through the centralization of treatment, experience would be enriched and the treatment itself possibly still further improved, thus increasing the number of successful cures. Such hospitals would provide other hospitals with a steady supply of physicians, well-trained in the Sakel Insulin Shock Therapy, who could then develop the treatment and prepare the way for an active therapy of mental diseases, which would convince the public of its worthwhileness.

Nor would such hospitals be an additional expense to the state. On the contrary, millions of dollars would be saved because so many of the patients who are now confined for life would not only be discharged, but would be able to undertake productive and gainful occupations.

Material considerations are insignificant in comparison with the purely human tragedy which insanity represents. Roughly 20,000 new victims are claimed every year in the United States, and except for the handful that is being cured, all these, and most of them are young, are doomed to accept a fate which is often and justly said to be worse than death.

These facts are a challenge to all of us. Not all these victims are compelled to suffer this fate as they were in the past. Today the indifference and negligence of their fellow men are responsible for their plight. Literally thousands of them could be rescued every year. Something can be done, therefore it must be done. If there were no hope, no treatment, no cure for these, we would have no guilt, but for years there has been a treatment which offers a restoration of a very high percentage. Psychiatry will only advance as their case advances from despair to restoration.

I have given so much space to the record of the original Sakel Shock Treatment, that I introduced, in order to show clearly that when it is properly applied a high percentage of the sick can be reclaimed and that this percentage can be increased still further. I also wanted to indicate that the reason this has not been done and that no strenuous effort is being made even in these present times lies in the distortion of my treatment by those who claimed that a part of it, the convulsive factor, was an independent "new" treatment. Their sole justification in doing this was its simplicity and their urge to claim unwarranted personal "discoveries."

The welfare of the sick must override any personal considerations and ambitions. Mental patients are delivered to us in trust, and because they cannot speak for themselves, we have a greater obligation to them than in any other branch of medicine.

The helplessness, which has lasted for centuries longer than in any other branch of medicine, to apply a specific helpful treatment, has led to the intolerable situation where dialecticism was to become a substitute for scientific knowledge. The first ray of a helpful experimental treatment came with my proposal for a physiological treatment by means of insulin overdosage in 1927. It had a hard time to be brought into the light and an even harder time to override the strong established scholasticism, but it is a well-known fact that it always takes a hard uphill struggle to establish even a proved successful treatment against the law of inertia, which is on the side of an ingrained opposition.

For these reasons I am putting before you at this late date, not my claims, but the claims of the thousands of sick, who could have been helped and were not, and of those countless thousands to come, who still could be saved and who will be lost unless the original true record of the inception of the Sakel Shock Treatment and the results of the last 27 years are studied with scientific impartiality and without consideration of personalities. Only then can the Road to Rescue be recharted.

The time has come when further silence on my part with regard to the aimless deviations from the original Sakel Shock Therapy is not only unjustifiable but altogether unpardonable. Hitherto, I have only published when I felt I could submit for examination something that was tried and well-founded, and I have waited too long a time in order to verify the correctness of the therapy I wanted to recommend. I thought it was enough for me to show

the way and that the rest would develop naturally in accordance with the law of the survival of the best. Evidently, I should have acted differently.

I will attempt to give here the latest therapeutic method which, based on my more recent experience, I am convinced is the best available today. I hope that it will clarify the existing widespread misunderstandings and correct the deeply ingrained false conception and misapplication of the various component parts of the original shock therapy.

Here again, as in my book *The Pharmacological Shock Treatment of Schizophrenia*, I must call attention to the fact that I do not presume insulin to be a "cure-all" remedy, nor that the interacting psychological factor in psychiatric illnesses must not be concurrently treated by psychological means. Insulin is doubtless only one of many still unknown agencies whose hormonal, metabolic and neurotropic properties can serve to rectify intrinsically endogenous malfunctions. Up until now, however, it is the only one sufficiently well-known to be used with any degree of empirically justified scientific accuracy, and it has proved a sufficiently successful tool to warrant not only its present use, but further exploration. But it must be emphasized that the effect of its use depends not so much on the tool itself, as on the man who wields it—his training, experience, and knowledge. The application of the treatment requires not only considerable psychiatric knowledge, but equally, a knowledge of physiological, experimental, and internal medicine.

In defining endogenous nervous-mental-emotional diseases, it is necessary to differentiate them as clearly as possible from the environmental or culturally typical distortions of the personality and not to view them as diseases in the medical sense. Psychological rehabilitation has its place in the practise of all the various medical disciplines. Where the major problem is pathopsychological maladjustment, like a complex, which yields to the psychological skill of the therapist, medical means to deal with the situation would be used only as an adjunct to strengthen the nervous structure of the patient in order to enable him to endure the assault of psychologically adverse circumstances with less wear and tear. In cases of true psychiatric diseases, this emphasis is exactly reversed.

There are four, clinically recognized, psychiatric disease groups which must definitely be considered as malfunctions of the central nervous system. They are:

1. The underlying dysfunction found in the group of psychopathic and psychoasthenic conditions, which includes anxieties, neurosis, compulsions, and major addictions of all kinds and which cannot be dealt with by the simple expedient of removing their circumstantial or environmental cause.
2. The disease group of cyclothemia, better known as manic-depressive or periodic disturbances of the emotions, which can exist without impairment or involvement of the mental functions.
3. The group of malignant involutional melancholias in their different manifestations, leaning towards the simple cyclothemias on the one hand and towards the group of schizophrenic malfunctions on the other.
4. The group of diseases exhibiting the schizophrenic symptom complex, which indicates clinically the presence of the typical schizophrenic primary process, according to the patient's innate individuality, the incidental circumstances of the time,

and his temporary preoccupation. This primary process will manifest itself in the various distinct components, the totality of which comprises the personality. The schizophrenic reaction types correspond to the disfunctions of one or all of these components and can be classified as follows:

a. paranoid group
b. catatonic excitement with paranoid tendencies
c. catatonic stupor, negative or positive, with mutism and flexibility cerea
d. schizophrenia simplex with an insidious beginning
e. hebephrenia

The treatment for these diseases consists in the flexible and individualized use of many adaptable techniques which must in no case be perfunctorily performed, because the treatment has to repair the most conspicuously malfunctioning part of the personality. Before analyzing these in detail, I wish to give an outline of the Sakel Insulin Shock Therapy and of the theory which led to it.

I started to use the new approach in 1927, applying it to the simplest psychiatric cases and I called it the "Borderline Treatment." I selected the name "Borderline" because of the fact that I strove by means of insulin to induce in patients a marginal hypoglycemia and hyperinsulinaemia that was deep enough to be therapeutically rewarding, while yet avoiding the extreme manifestation of the shock. I avoided the coma-hibernation and the convulsion by all means available in the preliminary group of test patients.

The current profusion of labels by which it is called today grew out of my own inability in the beginning to settle on a definite name for it. In the first publication in 1928, I called it simply "neue Behandlung" (new treatment). Subsequently, in 1933 I spoke about the intensified treatment for psychosis as Shock Treatment, "Hypoglykemiebandlung" (hypoglycemic shock treatment) or "Schocktherapie" for short. Still later as "Classical Insulin Shock Treatment," "Pharmacological Shock Treatment," and finally "Sakel Treatment." To add to the confusion, such names as "convulsive therapy," "subcoma treatment," and "fit therapy," appeared in literature along with other similar ones, more expressive of their author's particular bias or use of different drugs than the treatment as a whole.

I used this Borderline Treatment in cases of addiction and all kinds of neuroses. I started usually with 10 units of insulin to explore the individual patient's clinical reaction to it. Guided by the clinical symptoms, I then steadily increased the dose between 5 and 10 units each consecutive day. At this time, I did not exceed 40 to 50 units at each injection. Later, when protamine zinc became available, I used that where prolonged pacification of the patient was desirable.

During the first two weeks of applying this treatment, many unintended shocks appeared with random comas and convulsions. All the experiences I had gathered in my extensive animal experiments did not apply to man. I had found that with the white mouse, the insulin dose produced a 100 per cent response in a convulsion, and that by adding barbiturate to the insulin I could change the exclusively convulsive type of shock into a coma. Man, on the contrary, did not respond nearly as often to excessive doses of insulin with the

convulsion. The opposite reaction seemed to occur. But convulsions nevertheless did occur whether I added barbiturates to the insulin or not.

At this stage, during the first two weeks of my experiments with man, either shock, convulsion, or coma appeared as an accident. Fortunately, these occurred more frequently than I intended, and the discomfort of being confronted with a dangerous situation was soon counterbalanced by the realization of their relative harmlessness and by the extraordinarily gratifying results. I noticed that the whole personality of the patient, and at that time I was dealing only with neurotics and psychopathics, was dramatically changed after each convulsion.

These dramatic, instantaneous and hitherto unknown changes in the personality of the patient occurred with the regularity and infallability of an established formula. I therefore felt justified in now using the supreme and severe insulin shock in the form of convulsion or coma in the treatment of much more serious psychiatric ailments. Under the influence of the prevailing views of the doctors about insulin shocks, I attempted to develop a less hazardous mode of procedure which would tip the scales in favor of the treatment by increasing the beneficial effect and decreasing the danger to the patient.

The method of shock I started to employ on, to be exact, the sixth of June, 1927, is published in my subsequent serials, as well as in my monograph as the "Classical Insulin Shock Treatment" or, as I use it now, "Sakel Treatment." I called it "Sakel Treatment" for the express purpose of differentiating it from the indiscriminate and perfunctory usage of injecting insulin and neutralizing it according to any arbitrarily established rules with glucose. This was and is a hit or miss treatment and led to dangerous consequences, particularly when it was a "hit." Each physician, who had by accident achieved a good result, was tempted to apply his perfunctory performance in all cases. The natural outcome of this was that in many cases he was bound to suffer defeat due to his lack of knowledge and inability to adapt the treatment to each individual case. This was the danger I particularly sought to avoid.

In 1936 I said, "The insulin treatment has to be considered like the scalpel in the hands of a surgeon. The scalpel does not perform the successful operation. The skilful hand and the thinking and experienced brain of the surgeon behind it is responsible for its success." So it is with the treatment, particularly if the maximum efficacy and the highest percentage of success is desired.

I brought the treatment into a schematic broad outline for application in treating major psychiatric disorders. There were four phases as I outlined them in my lecture of 1933.

1. Phase I—Adaptation Phase: This phase started in the same way as the Borderline technique, but in many cases it was just the first step in the process of ascertaining the greatly varying individual dosage of insulin which was required to induce in the patient either one of the two kinds of shock, convulsion or coma-hibernation. The endurance of the patient also had to be determined, that is, the intensity of the shock which he could bear without danger, as well as the length of time of the coma, if a coma occurred which he could tolerate with safety.

2. Phase II—the Shock Phase: (I quote from my "Pharmacological Shock Treatment of

Schizophrenia" published in 1933 and in English in 1938): "This consists of the production of severe hypoglycemic shocks. These occur when the doses in Phase I are high enough or when the hypoglycemic period is sufficiently prolonged to produce a severe reaction. This shock may consist of either the coma or an epileptic seizure. In the former case the shock starts with profuse perspiration and progressive somnolence. It may be interrupted by psychotic exictement but ends typically in coma, which usually occurs in the fourth hour following the injection of insulin.

"The coma may attain a varying depth. In the initial stages the reflexes are still intact and energetic commands can rouse the patient's swallowing reflexes to the point where he can swallow food. But as the coma deepens the reflexes become pathological and finally disappear. The patient first shows positive Babinski, Oppenheim and Mendel-Bechterew reflexes; but later the coma may become so deep that all reflexes disappear, including the corneal and swallowing reflexes. The picture is one of complete areflexia with complete atonia of the entire musculature.

"In the course of such a 'wet' shock (coma-hibernation), brief muscular spasms of one or more of the extremities, or fine or coarse myclonic twitchings, or an intense tremor of the entire body may appear. Where the course of such a shock is smooth and without complication, a marked bradycardia develops and the pulse rate may drop to as low as 34 beats a minute. The temperature may descend to 30° C (89.6° F).

"Alternately, the less frequent 'dry' shock (convulsion) may develop. This consists of sudden, severe and typical epileptic seizure with tonic and clonic spasms, tongue bite, and sometimes a weak pulse. The convulsion may appear without any easily detectable premonitory symptoms.

"The depth and severity of the 'wet' shock can be regulated at will by postponing sugar administration.

"The typical 'dry' shock occurs in the second or third hour after the injection, in contrast to the coma, which occurs about the fourth hour. It is self-evident, that when the seizure occurs, the therapeutic effect of that particular hypoglycemic state has been achieved and the hypoglycemia should be terminated soon after the convulsion has occurred. The patient should be given an adequate amount of carbohydrates, despite the fact that he may have been roused from the somnolence by the convulsion itself, and the hypoglycemic state should not be allowed to progress much further.

"There are two types of epileptic convulsion in insulin hypoglycemia: the 'dry' shock or early epileptic seizure which occurs in the second or third hour, and the late epileptic seizure which occurs in the fourth or fifth hour of hypoglycemia and not infrequently in the course of the 'wet' shock.

"The late convulsion must be regarded as a danger signal and should be interrupted with intravenous glucose. The patient in this case does not ordinarily rouse from somnolence but may develop a status epilepticus, since the original state of irritation of the cell persists due to the protracted hypoglycemia.

"After having enlarged my experience in the past few years, it is possible to indicate how the basic method can and should be modified by regulating the duration of the hypo-

glycemia and the depth of the coma in the case of 'wet' shocks. The course of the 'dry' shock, since it is of short duration, cannot be changed. But it is possible to avert a 'dry' shock and thereby facilitate the development of a 'wet' shock if such a course seems desirable. On the other hand, the 'dry' shock may be deliberately provoked by pharmacological means, such as the administration of camphor or metrazol.

"The exact point at which the hypoglycemic period is terminated is of great importance. It is dependent to a certain degree upon the self-regulatory (mostly the hormonal-metabolic) activity of the organism but mainly upon psychiatric factors. These considerations to the 'dry' shock or epileptic type of reaction, which has to take its course, could not be applied.

"When once the insulin dose is found which produces the desired hypoglycemic shock (coma or convulsion) in any one case, the dose is repeated as long as the same reaction is achieved. There is, as a rule, a tendency for patients to react with the same intensity when the dose has been found.

"The hypoglycemic shock if properly administered and supervised is less of a strain on patients than its previously exaggerated dangers would have led one to expect. This makes it possible to eliminate Phase III, the rest phase, as the case requires and to treat patients daily or every second day with insulin shock provided that the physical condition allows it and the mental condition requires it. At least one rest day a week is necessary.

"Phase II ought not to be thought of as a circumscribed period in which the psychosis is radically or suddenly cured with one or with a set number of shocks, but rather as a period of progressive cumulative action which shows results only after a certain period of time. Too short a treatment is less a safeguard against relapse than a long treatment. Overlong treatment may also prove harmful. The physician's decision based on his experience are consequently of the utmost importance.

"Phase II consists of the daily administration of about 40 to 200 or more units of insulin by deep intramuscular injection. The size of the dose depends on the amount necessary to produce shock in any given patient. When once the shock dose is found the depth of the coma depends only upon the duration of the hypoglycemia.

"On the first day of treatment, for example, a patient was given 20 units of insulin, fasting at 7 a.m. In four or five hours he showed no marked reaction and was given some carbohydrates. He ate his lunch soon afterwards, at say, one o'clock. No further doses were given unless the patient was unduly excited and needed insulin as a sedative. In this illustrative case the following doses were given:

On the second day, a single dose of 30 units of insulin
On the third day, a single dose of 40 units of insulin
On the fourth day, a single dose of 50 units of insulin
On the fifth day, a single dose of 55 units of insulin
On the sixth day, a single dose of 60 units of insulin
On the seventh day, a single dose of 70 units of insulin

In each case, food was withheld for at least five hours after the injection. Up to now there was no shock reaction. On the eighth day the patient got an additional 10 units. Four

hours later, he became somewhat somnolent but could be aroused with difficulty on command. On the ninth day he got 90 units of insulin and went into coma-hibernation three hours after the injection. The coma was permitted to deepen for one-half to one and one-half hours before carbohydrates were administered so that the coma should attain the depth desired in this case. If the patient develops a 'dry' shock, then the hypoglycemia should be terminated soon after by means of carbohydrate administration through a nasal tube.

"The same dose, 90 units, was repeated on the following days, early in the morning to produce the desired depth and intensity of shock. If the response was inadequate, the dose was increased by five or ten units the next day. But it was often possible to reduce the dose and still attain the desired effect.

"Shocks of this type are produced once a day with at least one day of rest a week until the desired therapeutic effect is obtained and the patient shows no psychotic symptoms either during or after the hypoglycemia.

3. "Phase III is the period of rest during which the patient is given no insulin or never more than is essential to pacify him.

4. "Phase IV—the terminal or polarization phase is short and may last from four to eight days during which 30 to 40 units of insulin are administered once a day. These are given to produce borderline physical signs of hypoglycemia. Due consideration must be given to any hypersensitivity or diminished sensitivity to insulin which has appeared in the meantime. In any case carbohydrates should not be administered later than two hours after the injection in this phase. In some cases this phase may be entirely omitted."

This was the procedure of the treatment I started to use in 1927, and presented in 1933. I already emphasized then that it is not a rigid formula, and during the lecture I demonstrated cases in which I had achieved the severest convulsive shocks with 30 units of insulin and others which had shown no reaction at all to 370 units. Such situations made me particularly anxious to stress the pitfalls involved in a perfunctory application of the treatment. I also indicated that it was not necessary to consider the four phases of the treatment as inseparable from each other. Improvement and even recovery can occur by employing phase I only, which is the same as phase IV, and which is now known as the subcoma or subshock treatment. Unfortunately, there has been a tendency to apply this perfunctorily as a treatment by itself in all cases, regardless of whether or not the cure fits the patient. The application of variations of the Sakel Treatment to neuroses and other forms of psychiatric illnesses was hardly mentioned at that time, because I thought it of the utmost importance to center the attention of the doctor on the fact that a treatment had finally been found for the hitherto incurable disease, schizophrenia.

It is necessary here to point out that the Sakel Treatment has proved much less dangerous than originally anticipated. Dangerous complications or fatalities did not and do not at any time exceed in my experience the lower approximation of 2 per cent. This chance of complication is equal to a simple chance one takes in an appendectomy. Certainly no one considers an appendectomy as a serious operation with exaggerated complications of fatality today. At the *advent* of surgical appendectomy the percentage of fatality was high, the danger of the operation great. As time progressed surgeons continuously acquired greater

knowledge and experience. They imparted this to the next generation of surgeons as well as their learning from mistakes and teaching to avoid them. No generation of succeeding surgeons were permitted to start on their own and to renew and continue the old errors by their own trials. Surgeons were forced to acquire their mastery in a rigid and complete apprenticeship. This logical procedure in an experimental medicine led to the fact that appendectomy became a harmless surgical performance.

Unfortunately the opposite can be said about the teaching and application of the Sakel Treatment. Basically in its beneficial and dangerous implication it can be rightly compared with the above mentioned surgical performance. Unfortunately superficially it appeared simple. To the uninitiated all that it seemed to be was to inject a given amount of insulin and later on to give the patient carbohydrates. To a physician or nurse, lacking the basic apprenticeship for this treatment, the extraordinary successive stages of physiological changes following the insulin injection were unknown and unfortunately dramatically invisible. Such therapists seemed to be at ease and thus at liberty to change the rules of hard won experimental advice outlined by me. Some of them changed the length of insulin hypoglycemia or depths of coma and lost ultimately by doing so the chance of a possible cure. Some changed my advice of finding the individual insulin doses in the patients by unwarranted and excessive sudden increase and by doing so multiplied the danger of fatality of the treatment. The fact that some patients become sensitized to insulin during the treatment and the individual dosage in such cases could be decreased misled some to a reversal of my original outline for it. Instead of feeling their way gradually in each individual case and increasing after 90 units of insulin, as I advised not more than 10 per cent, in the next dosage they started with a high dosage and wrongly raised the dosage from case to case. The outcome was a possibly convenient shortening of the phase 1, but unfortunately a dangerous unnecessary overdosing of each patient in the shock stage. Even if they could, in the majority of patients, rectify the situation by reducing the dosages to the optimal minimum one from the excessive and unwarranted high one, it does not eliminate the fact that by doing so they were bound in some cases invariably not to be able to escape the danger they created by overdoses. Thus much more frequently than necessary dangerous and fatal complications occurred. They added to the alarming rise of the percentage of fatalities by their "modification" of starting with overdosages and then declining with the dosage which they misconceived as a natural adjustment due to "oversensitivity." The Sakel Treatment, due to such a modification, became without justification known as more dangerous and more complicated than it really is when properly executed. This can be parallelled by "modifications" of eliciting and isolating convulsions only in treating schizophrenia, where another danger was created, the differences of the danger being that less cures were procured instead of more fatalities as in the above mentioned "modifications."

The trend that developed should have been foreseen but was not, and, as I have said before, I must confess myself guilty of prematurely emphasizing the value of the convulsion in schizophrenia and thus opening the flood gates to the distortion of the treatment.

After 27 years practising, searching and experimenting, I am now in a better position to evaluate the specificity of the various factors contained in this intricate treatment and

their therapeutic affinity for the different and separate psychiatric diseases and conditions. I am no longer at the stage of "groping," nor do I have to depend upon "intuition" to know when to apply a convulsion or a coma, what length or depth the latter should reach, and when to take decisions with regard to the various durations of the hypoglycemia in the so-called subshock or subcoma treatment.

I propose to discuss briefly, as I have only a limited space available, an outline of my latest modifications with which I seem not only to hold to my original high percentage of good results but to achieve a higher one. In order to understand these better and to consider the treatment against some kind of background, I shall include a review of the theory which will, I hope, enable the reader to grasp the differentiation of the treatments and theory as a concerted whole. My original conception of the physiopsychological attack upon psychosis has been confirmed by experience. The theory underlying it still remains hypothetical and flexible but it has established itself as a working hypothesis.

In discussing the purely physical metabolic diseases of the nervous system, it should be borne in mind that psychiatric medicine cannot exist without taking into consideration the neurological substrata which, as an organ, is the basis of thinking and feeling. To consider the problems of psychiatry in an abstract sense alone would be analogous to dealing with the grin without the cat. It is difficult, however, to define the metabolic diseases of the nerve cell since we do not know what Life really is, nor are we able to discern fully the complicated intrinsic process in the interplay between the metabolic action of the nerve cells and their reverberating action upon themselves by means of various forms of energy and force, some of which are known and others unknown.

It should be remembered that though there is an anatomical distinction between the central nervous system and the autonomous nervous system, clinically they are somewhere and somehow closely linked together.

In addition, all vital functions of the body are directed by the vegetative or autonomous nervous system. As we now know, the governing influence of this system influences the glands producing the various hormones or catalysts, which in turn maintain the stability of the metabolic processes of their governing nervous cell system.

What we understand by metabolic processes is the force which transforms the chemicals, ingested in the form of food or oxygen, into a different form of energy which is able to support and maintain life in the living organism. It must also serve to build, sustain, and replace the structure of the living cell, which alone is capable of transforming energy into life processes, life tissue and even thoughts. The metabolic processes of the cell have a dual purpose: to convert fuel and life energy in order to support the living function and to construct matter from energy in order to repair and replace the structural "machinery" of the cell and so keep it in working condition.

The fuel consumed in metabolism constitutes the same organic chemical substance as the material which comprises the cell. The metabolic process, therefore, involves the consumption of the actual material of the nerve cell and, with time, uses it up. This is the natural process which manifests itself in the determination of the life span of the normal cell and the life span of the person.

Since the metabolic process has two functions, it is understandable that it can produce two distinct clinical changes. These are: (1) a change in the function of the cell but one which does not interfere with that part of the metabolic process that is directed toward the structural maintenance of the cell; (2) a change which impairs the ability of the metabolism to make the repairs necessary for the maintenance of constancy in the structure of the cell. It is obvious that when the first change occurs, it is remediable and does not result in an organic damage. When the second one occurs, it will remain irreversible and permanent, whether the damage done is due to the nature of the change or its duration.

Metabolic diseases in the nervous system have to be completely differentiated from diseases caused by an outside infection (psychological injuries excepted) in which the invading organism feeds on and destroys the nerve cell. In metabolic diseases no outside attack upon the nerve cell occurs.

Three possibilities of disturbances causing metabolic diseases can be traced:

1. Dietary: such as avitaminoses, alcoholism, ingestion or inhalation of poisons affecting the normal metabolism.
2. Long standing addiction: such as to opium and hashish, which in time induce toxic traumas to the nerve cells equal to those that are sustained in occupations involving exposure to arsenic, lead, etc.
3. An acute metabolic disturbance, spontaneous or artificially induced via psychological prolonged traumas, resulting in endocrinological changes like thyrotoxicosis, diabetic neuritis, or insulin hypoglycemic convulsions or comas which may cause irreversible damage.

The metabolic diseases that result from these causes can be cured by removing the source of the disturbance. Since the nerve cell uses carbohydrates as the fuel which enables it to discharge its metabolic function, an acceleration of the restorative process can be achieved by including an increase in the active carbohydrate metabolism. Insulin and/or thiamin can be used to induce this curative increase. Insulin not only stimulates and improves the metabolism, thus helping the nerve cells to a quicker restitution of their function, but it also serves to reinforce the nerve cell by forcing it to store glycogen. The symptomatology of the artificially induced insulin hypoglycemia has to be very carefully defined, since it is possible to overreach the therapeutic limit and to cause permanent damage.

Experience has shown that in insulin hypoglycemia there is a definite period during which the metabolism of the nerve cell is interfered with but capable of being restored to normal if properly handled. This is the period during which insulin is affecting only the functional part of the metabolism and does not trespass on the part which is concerned with the maintenance of the healthy structure of the cell.

An artificial hypoglycemia of deep severity can be neutralized by the application of a sufficient quantity of carbohydrates if applied in time. For example, the deepest coma, showing the whole battery of pathological reflexes from Babinski to decerebration symptoms, will disappear after a timely intravenous glucose injection. If a coma or convulsion is permitted to endure beyond the therapeutic tolerance point, irreversible structural, anatomical damage will occur. The length of this therapeutic time limit varies in individual patients

from four to seven hours. Consequently great skill and experience on the part of the physician is required. In old cases of schizophrenia, where the Classical Sakel Treatment has been of no use, the coma may be protracted beyond the safety limit. Needless to say, this is very dangerous, but if properly directed, it can achieve a cure. This latter treatment rests on the assumption that the diseased and therefore weakened nerve cells will die off first, from the effects of the hypoglycemia, before the healthy ones are traumatized. This selective elimination of the diseased cells leaves the healthy ones a free field in which to resume their normal performance.

An example to illustrate this "exception to the general rule" might elucidate this point: A patient, who had already been institutionalized for some years for schizophrenia, came under my care. His case history revealed that he had been ill for a long period prior to the time when confinement became unavoidable. When I received him, he was in an advanced state of deterioration, spending most of his time in the institution in a straight jacket. The prognosis seemed hopeless during the one year in which, under my care, he was treated with the Classical Sakel Treatment. Before giving up further treatment as hopeless, I decided, with the consent of his family, to try the dangerous "prolonged" coma. The patient showed a great resistance toward insulin and needed very large doses to produce a shock. I increased the dosage to 1,800 units of insulin without at any time achieving either a deep coma or a convulsion. The 1,800 units were administered daily for six weeks without effect, pointing to the explanation that the antagonistic adrenocortical system had become conditioned to this amount of insulin and so had come reflexively to neutralize it. At the end of six weeks, I dropped the dosage from 1,800 to 600 units from one day to the next. My explanation is that because the adrenocortical system was caught unaware, the patient reacted with the severest kind of insulin coma. When carbohydrate was administered both orally and intravenously five hours after the 600 units of insulin had been injected (which was a half hour sooner than it had been given during the period of the 1,800 units injections), the patient failed to rouse from his coma. He continued to have complete areflexia and decerebration symptoms for 24 hours. Babinski appeared and moderate pupil reactions to light started to reappear after this time. Step by step, over a period of 12 hours, the patient gradually awoke. The general state was one of pleasant calm with an amnesic-aphasic manner, shown by the lack of relevant response to some of the questions asked him. After five days, all pathological reflexes disappeared. The patient was able to leave his bed for the first time in years without being forced to do so. He was able to take care of himself, to dress and carry on a completely normal conversation, though he had an amnesia covering the whole period of his sickness. He continued, after his discharge, to be perfectly normal and well, resuming family, marital, and community obligations and relations.

Treatment of this sort seems to me to bring about permanent, selective, structural elimination of diseased nerve cells through metabolic interference.

In contrast to this, treatment by the classical Sakel Insulin Method is confined to affecting only the transient pathophysiological and therefore reversible metabolic processes in patients with sickness of a short duration. During the period of reversibility of the insulin hypo-

glycemia and because of the insulin, the metabolic diminution of activity in the nervous cells represses with time that portion of the diseased nerve cells which happens to be the most active at the time. This allows the dormant healthy cells to be activated and achieve dominance over the formerly disturbed portion. Years of experience have confirmed my basic assumption that the metabolic changes due to hypoglycemia repress the mental and neurological condition, regardless of whether the condition at that time would be considered normal or abnormal. They give the malfunctioning cells an opportunity to recover during the period of hibernation. When the metabolic restriction imposed by the insulin hypoglycemia starts to take effect, the functions of the central nervous system are diminished, and even completely eliminated step by step to the point of hibernation in a regular philogenetic order. The patient will at first become somnolent but with all neurological reactions still intact. As the coma deepens, the reflexes become pathological and finally disappear. The patient will show positive Babinski, Oppenheim, and Mendel-Bechterew reflexes at first, but later the coma may become so deep that all the reflexes, including the pathological ones, disappear. The termination of hypoglycemia through the administration of carbohydrates reverses this progression in exact inverse order.

During the process of the awakening, one can actually see a return, level by level, of the functions of the brain layers in a progressively higher order, as I described it in my original publication. At first the less sensitive layers of the brain are aroused, apparently because, being the older and more primitive centers they are more resistant to the metabolic nutritional deprivation of the hypoglycemia. Even a slight rise in the blood sugar will be sufficient to activate them. The reflexes appear, first pathological and then normal. Normal swallowing is the last reflex to appear. The sensory and motor centers are gradually aroused too, according to the same pattern.

It seems as if the brain centers, whether they have been eliminated or blockaded by the hypoglycemic restriction of the metabolism, are progressively reactivated by the restoration of the metabolic level in direct relation to their degree of resistance to deprivation of nutrition and the modesty of their metabolic demands. The philogenetically most recent, and therefore most vulnerable, are the last to be revived.

The use of a method, such as insulin therapy, which allows for the control and manipulation of the metabolic processes for therapeutic purposes, must not be confused with ersatz methods that superficially seem to be identical with it because the external symptoms are somewhat the same. The "shocks" induced by means other than insulin show clinically, but only superficially, the same picture for the critical reason that they are not controllable. They affect the structural build of the cell and are therefore more likely to impair than to help that part of the metabolism which serves to maintain the structure of the cell. This is particularly evident in patients who, after the application of many electroshocks, exhibit retrograde amnesia, slap-happiness and irritability, in addition to definite impairment of mental and emotional functions. To achieve this state can hardly be considered a satisfactory outcome of a supposedly therapeutic treatment.

The vital importance of the proper use of the therapeutically intended metabolic changes must be re-emphasized. Great harm can be done by improper application, since it can pro-

duce irreversible structural damage to all the nerve cells indiscriminately, instead of securing the selective elimination of the diseased cells only.

It might be as well at this point to recall the distinction I made earlier in the paper, between the "early" spontaneous convulsion and the "late" spontaneous convulsion in insulin hypoglycemia. The "early" convulsion which comes between the second and third hour is a sort of defense mechanism, a reflex, centered in the midbrain to combat the hypoglycemia. It is therefore useful and without bad aftereffects.

The "late" convulsion, occurring in the fourth to fifth hour, seems to originate directly in the overirritated cortical brain cells. It indicates the danger limit of the incipient or already well-established, universal, structural nerve cell damage. It must therefore be put in the same category as any other traumatic irritation to the cortical nerve cells.

This can be demonstrated clinically by the fact that the patient returns quickly to consciousness and normal reflex actions after an early insulin convulsion. In a late convulsion, the patient shows much longer, more persistent pathological reflexes and prolonged retrograde amnesia, such as are apparent in other generalized traumas to the brain cortex, for example, in concussion, electroconvulsion and other nonselective brain cell damage.

We are still far from the point where we can say that we understand definitely which physiological, metabolic considerations ought to guide us in the choice of any of the many possible variations of the pharmacological metabolic or physiological electrotherapy in their application to any one clinical condition. One should, however, strive to produce as little structural damage to the cell as possible.

The conception of a physiological foundation of mental processes made it necessary for me to assume, for therapeutic purposes, different corresponding physiological disturbances as a basic cause for different psychotic symptom complexes, like schizophrenia and cyclothemia.

The interpretation of the mental (i.e., psychological and perceptive) strangeness and the changes appearing during a single insulin shock convinced me that the psychological syndrome characteristic of schizophrenia is caused by a dysfunction of the whole brain matter. The manifestation of such mental processes as well as the unconnected mental perception (hallucination) in schizophrenia differ basically from normal mental processes and are therefore different in quality.

In cyclothemia, which is a self-curative disease, the mental and emotional levels differ only quantatively from normal mental processes. Delusions in cyclothemia center about the psychotic process. They prove the intactness of the logical functioning of the brain. The patient, adhering to the unimpaired faculty of seeking cause and effect connection, has to invent a fictitious cause of his emotional distress. His delusions are the outcome of his emotional distress. In schizophrenia, in contrast to this, the emotional disturbance may be the primary or secondary result of the mental delusions.

In applying the shock treatment, it was necessary to determine in each case which of the two physiological disturbances was to be corrected at a given time and which adaptation of the treatment could do this most effectively. The procedure used to obtain the best therapeutic results includes at the present time a more exact knowledge of the special beneficial

effect upon affective psychosis of the convulsive shock factor which enables one to minimize the damaging aftereffect of the convulsion.

The therapeutic procedure which has proved to be best for affective psychosis is: the original insulin shock and the provocation of early convulsions in hypoglycemia, but in limited number. Amnesia is considered an undesirable by-product and is to be avoided if possible.

The therapeutic possibilities for chronic psychosis are:

1. "prolonged" treatment with the established procedure of insulin shock for a month.

2. "concentrated" treatment as I have already described it; the process of deliberately producing a number of "late" convulsions after the insulin coma has reached its maximum intensity.

3. prolonged coma.

The latest experience with the treatment of chronic cases has to be left for later and more detailed publication. The methods I am about to describe and which I have given in outline have proved to be the best available for schizophrenia at present.

I feel justified at this time in using the word "cure." I do so only by way of reaction to those leading psychiatrists who keep repeating, "I have still to see a cured schizophrenic." The reason that they are still bound by this belief is that they do not add to their unquestionable knowledge of that disease, the ability to appraise the quality of the treatment to which the patients are subjected and on the results of which their opinion is based. Their verdict is but another illustration of the lamentable fact that few insulin shock treatments are handled properly in the institutions which they often head.

I propose now to review all aspects of the original Sakel Insulin Treatment in their application to the various groups of mental, emotional, and nervous diseases.

The borderline insulin approach can be applied in all marginal cases, from simple physiological nervous exhaustion to the severest anxieties in neuroses, neurotic depressions, and even in mild psychotic conditions. In most cases the doses should start with 10 units of insulin, increasing the dose according to the patient, up to 40 units. Doses higher than this must be closely supervised until the hypoglycemia has been terminated in order to prevent an inadvertent shock. In cases which require prolonged pacification, plain insulin can be replaced by protamine zinc insulin to extend the effect.

The therapeutic results of the Borderline Insulin Treatment seem to be achieved mainly through the insulin hormone, which acts directly upon the autonomous nervous system. It appears to act through the metabolism as well. The small doses of insulin do two things: first, they reactivate the dormant nerve cells and secondly they make the weak ones more robust by forcing them to store glycogen which is apparently the only reserve energy that the nerve cell lives on. The clinical evidence so far accumulated substantiates this assumption. Patients treated in this way react after a while more normally and healthily towards the same set of abnormal and injurious environmental conditions. Some patients without any psychotherapeutic support—which is not to say that such support is superfluous—start little by little to cope with their problems and adapt themselves to the situation which they had previously reacted to in a completely inadequate so-called neurotic pattern.

The only possible explanation is that through the accumulation of glycogen the sum total of the nerve cells is strengthened and made sufficiently robust to cope with a given situation. The unfavorable psychological condition alone could not possibly be the sole factor responsible for these so-called breakdowns. There must exist a precondition consisting of a weak nerve cell system. The millions of people who underwent the cataclysm of the past decades in Europe and Asia must incontrovertibly prove this fact. The percentage of mental cases in such countries is not greater than the precentage of similar cases in nations which were spared these horrors. Every human being has a breaking point when confronted with unendurable circumstances, but this point is relative to the strength of the individual and to his ability to surmount it.

An additional benefit is derived from the catabolic effect of lowering the sensitivity of the patient through the blood sugar and through the shift in the mineral relations and the electrical potential. The restoration and strengthening of the nerve cells through the forced accumulation of glycogen reserve energy caused by the anabolic effect of the insulin is evident in a long treatment. The clinical records of this treatment show that the pacifying effect of insulin is only one factor of the whole treatment. After such a treatment, the improvements caused by the above-mentioned factors can be easily observed. The patient gradually begins to deal with the same set of psychological problems in an entirely different manner.

In more serious psychiatric conditions, which spring from disturbed in addition to weakened functions, the confusion of ideas in psychosis as well as anxieties caused by a pathological sense of urgency which lead to overstrained and confused thought associations, may, under the influence of insulin hypoglycemia, be restored to the normal state of intensity and calmness.

This improvement may not necessarily be lasting. The dominant psychotic or neurotic ideas and delusions may recede partially or completely, but, at the beginning, they recede only for a while. As the treatment continues, they are gradually replaced by normal, integrated, mental and emotional responses which accord with the patient's previous personality. At the same time the depleted reserve energy of the nerve cell is replenished by the glycogen storage, and the whole nervous system becomes stronger.

In cases where the Borderline Insulin Treatment does not suffice, its intensity can be increased by either increasing the insulin dosage or by prolonging the time of the influence of the same insulin dose and letting the hypoglycemia last for an hour and a half to a maximum of five hours. This procedure must be adapted to the needs of the individual patient and to his temporary mental or emotional condition which can alter from day to day.

It should be noted that in some cases of schizophrenia, the pacifying and restorative effect of the borderline treatment alone is highly satisfactory. It may even be able to arrest the schizophrenic primary process and induce the recovery of the patient. But in the vast majority of these cases, it is not adequate.

In cases where the borderline treatment does not suffice, it becomes Phase I of the Classical Sakel Insulin Shock Treatment.

In Phase II, where the treatment is intensified to produce a shock, the individual insulin dosage is already known. The individual tolerance for the continued duration of each hypo-

glycemia has to be watched daily in order that it may be reversed. The type of shock, convulsion or coma must also be determined daily. It will be noticed that the pacification of the patient will occur for short and then for increasingly longer periods before the shock ensues. As the treatment proceeds, the preshock reactions may be reversed. Where the patient was previously lucid and calm, he may now become agitated. The lucid period may appear after the shock has been terminated. It must be stressed that as long as the activation of psychotic or neurotic conditions occurs in hypoglycemia, or shortly after the termination of it, a lasting cure has not yet been achieved.

It may be helpful to reiterate the hypothetical assumption that such a condition may be due to the fact that during each insulin shock treatment, the action of the vital forces of the nerve cells is restricted because the cells are deprived of carbohydrates. Because the psychotically functioning nerve cells are the most active in the case of a psychiatric condition, they are more affected than the dormant reserve "normal" nerve cells by the insulin hypoglycemia–blockade. Due to the respite or hibernation period given them, these malfunctioning nerve cells will be sufficiently strengthened to follow their tendency to revert to normal functioning, or else they will be sufficiently weakened to force the normally dormant ones to take over permanently.

The most interesting aspect of the "activation of psychosis" is that the patient will reproduce with high fidelity, but with steadily diminishing intensity, a mirror-like picture of his previous psychotic, neurotic, or hallucinatory mental and emotional reactions. It is reasonable to assume that the insulin "activates" the malfunctions causing these actions and eliminates them in the course of the treatment. As the treatment progresses favorably, the activation of psychosis turns into the above-mentioned reversal of reaction.

Two things in connection with the successful administration of this treatment must be remembered. One cause of very great harm to the patient is the faulty habit of terminating the hypoglycemia at a point during the shock before the moment of greatest therapeutic intensity. Secondly, though the Borderline Insulin Treatment has proved highly satisfactory in almost all psychiatric marginal conditions, a perfunctory use of the "mild shock" is not sufficient in the overwhelming majority of psychotic cases. It may result in the turning of a curable psychotic into a chronic one with greatly diminished chances of recovery.

At the present time I give Phase IV, the Polarization Phase, a position of greater importance. Consisting of somewhat smaller doses than the preshock ones, it is more apt to be successful even with schizophrenics of long duration. This form of treatment, applied over a long period of time, may arrest the primary schizophrenic process and produce a very slow but definite improvement.

The recovery of patients with long-entrenched neuroses, treated with borderline doses, follows a different pattern. The process of strengthening the energy reserve of the nerve cells, weakened by the excessive effort made to respond to vital functions, must be accompanied by an individualized psychotherapy. This will help the patient to reorientate his attitude and reaction to his psychological environmental problems and to stabilize his newly acquired adjustment after the successful erasure of his old patterns.

The preference treatment for schizophrenia, as well as for the groups of major psychoses,

is the insulin shock treatment which definitely incorporates Phase II. The two outstanding therapeutic factors of Phase II are still the convulsion and the coma-hibernation. These are now known to be applicable to different psychiatric conditions, the coma being valuable for the treatment of psychosis and the convulsion for emotional disturbances.

For therapeutic purposes, it is necessary to differentiate the reaction types in schizophrenia, since they represent pathophysiological conditions which apparently arise from different action centers of the central nervous system.

The first of these is the paranoid reaction type. In this type, the profoundest form of insulin coma has proven the most efficient and can be accepted as the treatment of choice. Convulsions, if set too often, are not only not beneficial but definitely harmful in this type. If convulsions are provoked, they must be kept to a minimum of between six and ten. The damage done is twofold. The convulsions result in a deceptive temporary amelioration of the condition, while the disease process continues unchecked, and secondly in anatomical injury caused by cortical overirritation. The faculties of association, logic and smooth thinking, which are usually preserved in paranoics, become aggravated and involved after such convulsive shocks because of the organic damage which gives rise to permanent irritation. This new defect is then incorporated into the patient's already irrational, tortuous paranoid system of persecution.

For the successful conduct of the Classical Insulin Shock Treatment without any additional adjuvants, the coma must be permitted to last as long as is consistent with physical safety and should not be terminated according to a fixed time limit for all patients. To terminate it too soon, is to avoid the possibility of physical danger but, at the same time, a great number of possible cures are lost. Such treatment must be repeated at least three times a week, in many cases six times until a successful outcome is achieved. It must be continued in the same intensity for at least four weeks after the patient has been restored to his former normal mental and emotional condition. If convulsions should appear spontaneously too often, they must be prevented by barbiturates given 10 hours before the insulin injection and by the elimination of all physical stimulation, like excessive light, noise, and unnecessary physical examination of the patient. Provocation of convulsion must be definitely restricted to those cases which remain resistant to large insulin doses for a long time and in which the varying of insulin doses does not provoke a coma.

Phase III in these cases, which is usually kept between 30 and 70 units, is allowed to continue for a longer time but is not always necessary.

The second type, the catatonic, must be separated for the purpose of successful treatment into three groups: (a)—Catatonic excitement; (b)—Catatonic "passive" stupor; (c)—Catatonic "active" stupor.

In the first group, the most promising application of the insulin shock treatment is to let the patient remain in insulin hypoglycemia only until the coma starts. Secondly, the coma should not be too profound or of too long duration since this not infrequently produces a relapse.

The progress of the treatment in these cases is more fitful and uneven than in the other and requires a longer time span. Convulsions should be kept to a minimum, although their harmful or beneficial effect is not as obvious as in cases of paranoia.

In some cases, the treatment with light insulin comas has to be alternated with deeper comas, in order to achieve a lasting improvement, but only after considerable reflection on the course of the disease.

Amelioration or cure may not become evident for many months after the termination of the treatment. This postponed therapeutic result may be called a "ripening process," a term which I have employed since 1933.

In the second group, that of "passive" catatonic stupor, the physiological treatment has to be carefully adapted to the individual situation.

Experience has proved that it is best to start with Phase I of the Classical Insulin Shock Treatment and proceed to Phase II. At the beginning of Phase II, it is propitious to let a light coma develop. It is essential to terminate the hypoglycemic shock at the height of its activation in order to consolidate the result.

It seems that in the majority of schizophrenic patients, the insulin hypoglycemia, in the stage before the onset of the coma, affects the predominant mental and emotional actions responsible for the clinical picture by subduing their morbid predominance. At the same time it affects, to a much lesser degree, the biological life process. By activating the dormant nerve cells apparently responsible for the reappearance of the normal, lucid period at this stage, it permits them to take over the functions of the previously dominant, diseased cells.

The second step in this procedure is to break through the stupor. Patients may awake with a little external prompting and may present a picture of complete reversion, that is of catatonic excitement instead of catatonic stupor. If this does not happen by itself, the coma should be terminated by a sudden intravenous glucose injection. Only if these two methods are unsuccessful should convulsions induced by metrazol or electricity be resorted to. The number of them should be limited to between 4 and 8.

Once the stupor has been broken, the next step is to convert it into a productive psychotic picture and thus make the other factors of the insulin hypoglycemia work towards a curative and restorative effect. The convulsion by itself has no such therapeutic effect. The symptoms may have disappeared, but the primary schizophrenic process remains. Therefore, the treatment must continue after the breaking through of the stupor has taken place. It must be discontinued only when it is evident to the therapist that no further improvement can take place.

The therapeutic procedure for the active catatonic stupor requires a fundamentally different approach to the use of the various therapeutic factors of the insulin shock treatment. The active catatonic stupor, which has the same appearance as a perceptive symptom as the passive one, has an entirely different dynamic mechanism. The active stupor is caused by the fact that the patient is laboring under a delusional command to persist in the forced inactivity of the stupor. Contrary to the passive catatonic process, he is not stuporous on account of a slackening of his biophysiological processes nor on account of his arrested thinking or emotional response. Such a stupor, therefore, will very seldom be broken by a convulsion.

In the majority of these cases, the application of the Classical Insulin Shock Treatment

without the provocation of convulsions has proved far superior to any other. It should follow the same course as that applied in cases of active, hallucinatory paranoics. Phase II has to be conducted to produce, slowly, a deep coma, which will progressively suppress and demolish the psychotic and delusionary product of the malfunctioning nerve cells. The diminishing intensity of this activity will encourage the resumption of normal mental and emotional functions. As the treatment progresses, the stupor will dissolve.

The convulsion in these cases would have numerous harmful effects. It does not have the transient value, as it does in cases of passive stupor, of breaking through the stupor. It aggravates not only the dominant symptomatic picture, but also the primary schizophrenic process. Moreover, it will add its damaging secondary effects to the burden borne by the nerve cells in their fight against the noxa causing the primary process. The expenditure of energy in the nerve cell, already taxed, will be increased by the convulsion and leave the nerve cell more depleted and possibly structurally damaged. This weakening of the defenses may come just at the time when a supreme effort is called for. There will be no energy left to accomplish a permanent restoration of the normal functioning. Furthermore, contrary to my original erroneous assumption, the amnesia caused by convulsion has no therapeutic value, because the psychotic condition is a manifestation of a pathophysiological nervous functioning and is not a psychologically confused problem complex. More explicitly, this psychotic content is nothing more than pathoplastic material derived from daily life and processed into distortion by the malfunctioning substrata which produce the distorted mental and emotional reactions.

The patients suffering from schizophrenia simplex must, from the therapeutic point of view, stand in a category by themselves. The diagnosis, in these cases, is usually made when the process of the disease has been long-established. The insidious beginning is so far back as to be untraceable. The patient is usually chronic by the time of the diagnosis, indicating very few psychotic pictures but always a distinctly blunted mental response, associative action, and judgment, which may be interspersed with mechanical rages and real or imagined emotional situations.

Treatment of this group will obviously be more difficult and the response less positive. Rehabilitation must be a corollary of the treatment, so that the patient can adjust to long-forgotten normal activities and ways of life.

Convulsion in these cases is of therapeutic value, because, by raising the emotional level of the patient, it is possible to stimulate the mental curiosity and activity which has been lost over a long period of time due to mental atrophy and deadened emotional response. But the number of convulsions must be carefully limited. Here too an excessive number will aggravate the inadequately functioning basic action of the nerve cells.

The most effective procedure in such cases seems to be the application for two to three months of the Classical Insulin Shock Treatment in order to strengthen the vital resistance and the self-defense potential of the damaged nerve cells by increased forced glycogen storage and increased functional activity of the dormant nerve cells.

After that period, convulsions may be provoked (not more than four to eight) by injecting metrazol intravenously, or if this is not possible, by electric current in the third or fourth

hour. This convulsive shock is intended to raise the emotional level of the patient. In difficult or unresponsive cases, it is sometimes helpful to provoke convulsions in the fifth or sixth hour of insulin hypoglycemia. This represents the so-called "intensive shock," where an attempt is made to add a convulsion to the coma. By this process, which has already been referred to, some nerve cells which cannot return to normal function are put permanently out of functional action, and the void thus established may force the dormant reserve cells, which have been strengthened by the long preparatory process, to awaken and take over. This late convulsion must only be resorted to in cases of extreme necessity and should, if possible, be provoked by metrazol rather than by electricity. From the beginning I used metrazol because electricity affects all the nerve cells indiscriminately, whereas metrazol is more likely to provoke the imminent midbrain convulsion.

Such a treatment is highly intricate and can be learned only by experience and not from the printed word. But if properly applied, it is highly rewarding and has made possible the reclamation of numerous cases which had been given up as hopeless by experienced psychiatrists.

In 1937 at the International Congress of Psychiatrists, I was able to show improvement and even functional recovery in cases which seemed completely deteriorated. The only possible explanation for achieving even short-term normalcy was that the brain works like any other vital organ, with only a fraction of its specific nerve cells assigned to its functions. The greater part remains dormant. If the "operational" part of the nerve cell group is diseased, the result will be distorted thoughts and psychotic reactions. The dormant reserve cells do not automatically take over to carry on the normal function. The process cannot be compared, therefore, with that of other vital organs.

It could be that the reason for this basic difference between the brain organ and other vital organs is that a disfunction of the active brain parts does not represent an immediate danger to life and does not, therefore, galvanize the reserve in order to save it.

It appears possible to activate the dormant cells only through the many component factors of the insulin hypoglycemic shock in all its phases. The hibernated cells are strengthened to the point of functioning during Phase I. Phase II suppresses the activity of the "psychotically" acting nerve cells. This seems to give a plausible explanation of the phenomena, already mentioned, of the transient lucidity in each hypoglycemia seen in the course of the insulin shock treatment in severe psychoses. Such a temporary lucidity increases in duration to the point of permanency in recovery as the treatment progresses.

Experiences leading to this hypothesis explain my attempt in 1934 at a possible selective elimination of nerve cells, that were diseased beyond recovery, in order to achieve a cure in old, chronic cases of schizophrenia. The results were excellent and have continued to be. They have justified the inherent risk of this drastic procedure. I have not published this technic in full, because I do not consider the material large enough nor the treatment safe enough to release it for application by insufficiently experienced and qualified physicians.

The recovery in cases properly treated with the more drastic method seemed to confirm the hypothesis that the dormant reserve nerve cells, so activated, can assume the functions of the distorted cells eliminated by the therapy which had formerly monopolized the mental activity with their malfunctioning distilling product.

Functional Disorders: To turn now from the schizophrenic to the depression group, the convulsion has proved itself of great therapeutic effectiveness in the treatment of involutional melancholia. Because this disease is apt to appear towards the end of a person's life, the slight impairments resulting from a convulsive treatment are not of such great significance as in young people, where a restoration of the mental processes to their former acuteness is desirable.

The best method is the Classical Insulin Shock Treatment. A convulsion should be provoked in the second to third hour of insulin hypoglycemia, achieving in all from four to eight convulsions. The therapeutic effect of any convulsion, induced by whatever means, is just as effective as the one provoked by forcing the insulin hypoglycemic state into a convulsive reaction. The routine procedure with involutional melancholia is to start with Phase I to find the individual insulin dosage and, forthwith, to provoke the essential but minimum number of convulsions.

There are, however, a number of cases that will not respond to convulsions. The treatment for this group must proceed with the simple classical treatment, where the coma prevails and the convulsion is omitted. Such patients are apparently much closer to a late schizophrenic primary process than to a malignant form of an emotional depression.

Timing is of extreme importance in provoking the convulsion, as proper timing may reduce the side effects to a minimum. A convulsion provoked in this manner resembles a spontaneous insulin midbrain convulsion in its clinical details. It is released in the midbrain, without undue irritation of the cortical cells, and, therefore, without the probability of even a slight damage to the pyramidal cortical cells. These are protected by the blockade caused through the cushioning effect of the insulin hypoglycemia acting as a shock absorber. The amnesia and confusion are reduced to a minimum. The emotional level is raised without loss of self-criticism or symptoms of euphoria. If the number of convulsions is kept to a minimum, the temporary impairment of the mental functions and haziness of the emotional responses will also be kept to a minimum. These desirable results are achieved more frequently when insulin as a medium of shock is used, than when metrazol or electricity is employed. This is because, the convulsive factor, though valuable in such cases, does not suffice to clear up the whole psychotic picture. In order to effect a cure or even an amelioration, it is imperative to bring into play the other factors which are contained in the insulin shock treatment.

The manic-depressive disease is a self-curative and self-limited one. It appears periodically and does not necessarily reappear. Whereas in severe schizophrenia, any risk taken is justified in the attempt to cure such a grave disease, the treatment of cyclothemia does not generally justify a drastic and possibly damaging treatment.

The manic-depressive disease involves emotional disturbances alone. Neither diagnostically nor therapeutically can it be placed in the group of mental diseases or major psychoses. The latter, as I said before, differ from the normal in quality, whereas manic-depression, as a purely emotional disease, is an expression of a disturbance in emotional response and in quantity to a psychological outer or inner stimulus and differs from the normal in degree only. To be happy or unhappy is a normal human function and is necessary for the pres-

ervation of the process of life, if the reactions are adequate and normal in relation to the demands of a given situation, whether physical, emotional, or environmental.

The basic difference between emotional disturbance and mental disturbance is that a mental one bears no relation to any normal occurrence in the life process, whereas emotional ones are only of proportion in the intensity of the reaction to a physiologically or psychologically justifiable situation.

In most cases of cyclothemia or manic-depression, the sadness is produced by no psychological provocation but by a disturbance in the "response" mechanism, located in the cycle center region of the brain, which regulates the normal function of being depressed or happy. The treatment of a depression cannot therefore consist of a psychological solution of a nonexistent "problem" nor of relieving any nonexistent psychological provocation. Since it is a medico-physiological disturbance, it must be approached by medical means.

To correct the "centrally" located disturbance in the region of the cyclic control centers of the brain, it must be reiterated that the precomatose insulin reaction usually causes a reversal of the prevailing emotional situation, apparently reversing the cycle. This action of reversing the emotional cycle can be used for the purpose of suppressing the depression and by acting upon the central nervous system, of releasing a euphoria instead. The prevailing emotional undertone may thus be permanently and successfully altered. An illustration of this is provided by the following two cases.

In a case of malignant depression, where the patient had spent five years in an institution, all treatments, having proved of no avail, she came under my care at the age of 64 years. The patient was treated with great caution and without great hope of success with the classical insulin treatment. Added care was taken because the patient suffered from a cardiac disorder and diabetes. In the sixth week of the treatment before the onset of a mild coma, the patient became hypomanic for a short time before returning to her depressed condition for the rest of the day. This process repeated itself four times. The sixth time, the patient lapsed into a coma from which she could not be roused for 11 hours, possibly because the excitation added to the insulin shock had put too much strain on her vascular condition. On waking, the patient was for the first time in a completely normal emotional condition. She remained well for three years, resumed her normal life with her family, and finally died of the heart condition, but in complete mental and emotional health.

The following case demonstrates how the insulin hypoglycemia can, in some cases, be used to reverse to normal the mechanism in the governing center of depression, where convulsions failed to do it.

The patient was a man over 60 who for the last two decades had had very frequent depressive episodes, increasing in gravity and duration and becoming increasingly frequent with the advance of age. At the age of 59, a new depressive episode reached serious proportions, unbearable for the patient and those around him. He underwent shock treatments by means of electric convulsions. The number of convulsions for one course was fourteen. His condition after these deteriorated, and his amnesia was profound. He came under my care six months after the last treatments with convulsions. The classical insulin shock treatment was applied with the intention of not forcing the shock into a convulsion. This

was necessary because of the patient's considerable memory defects and the proved therapeutic uselessness in his case of the previous convulsions. When the treatment was started, he showed clinical symptoms of defects in his thought processes—of the organic in addition to the depressive type. In the sixth week of treatment the patient showed, with ninety units, preshock symptoms. In the fourth hour, he became hypomanic and exhibited a reversal of his depressed condition. The hypoglycemia was interrupted at the height of its activation. This process was repeated for some time, but, as it proceeded, the hypomanic state little by little extended beyond the termination of the hypoglycemia. After two weeks it lasted the whole day. The patient was soon afterwards dismissed in a perfectly normal, emotionally sound condition without either depression or hypomania and with a marked improvement of his memory defects.

These two cases are not exceptional among the cases I have treated. They illustrate the fact that though convulsion is the treatment of choice in most depressions, it is not necessarily effective in all cases.

As a final example I quote the following case which I have selected because the patient himself is a physician and gave me his permission to print his case history. I am quoting it verbatim.

It was in the autumn of 1950, while in a state of mental depression and apathy which had persisted for six years, following several series of electric shock treatments for a Manic Depressive psychosis, when home for a week-end visit from the hospital which had given me domicile for five years, that my wife noticed a reference in the Sunday *Times* of October 1950, to a paper read by Dr. Manfred Sakel of New York City which was described as one of the "highlights" of the Psychiatric Congress then meeting in Paris. Doctor Sakel was sharply critical of the widespread use of Electric Shock Therapy, pointing out the temporary character of the patient's improvement under it and its frequent harm to the brain. Because he stressed the use of the Insulin Therapy as a means of restoring certain hormonal balances in the patient's system, with permanent results, we were hopeful that he might have something constructive to offer for my recovery.

My wife immediately wrote to him. He gave us an appointment and after seeing him and submitting each of us, a detailed history of my illness from the beginning, he assured us that the memory center had not been injured, but that communicating nerve fibrils—lines of association—undoubtedly had been harmed and rendered useless by the electric shock treatments. He went on to say, however, that with his new treatment, utilizing insulin once daily in small but precise doses and adjusting the time interval before the next meal, to obtain the optimal hypo-glycemic response and maintaining this level for the proper time interval, he was assured that this in time would stimulate the development of new memory association pathways and that eventually I would be able to resume the practice of medicine.

After following his prescribed treatment, I found that gradually in the fall of 1951, I was gaining confidence in some ability to recall events, persons, places, etc., from the past and began to yearn for work again if I could utilize my memory sufficiently to carry on.

Early in 1952, I received an announcement of some Post Graduate Sessions to be held in a mid-western Medica School starting in March, 1953. When I broached this plan to Dr. Sakel, he was somewhat reluctant for me to attempt it, believing that my memory improvement had so recently begun but he finally consented. So I started alone by train (the first time for seven years that I had travelled alone) on March 15, 1952 for the mid western university. Having previously matriculated for the six weeks course, it was with a sense of being born again that I anticipated my lectures and demonstrations there.

I found them instructive and illuminating after seven years away from practice so that my mornings and afternoons were full of scheduled classes and the evenings I spent in proof reading some manuscripts for Dr. Sakel, at lectures or at musical recitals. Sundays after church, I visited with friends of years ago and on twc

occasions went to nearby cities for dinner with medical school classmates and their families. Even a year before this, I would have been unable to do these things, held back by my inadequacy due to the extremely poor memory for names of people I had known, places at which I had been and general knowledge of events and medical terminology which had slipped into the limbo of the lost. Now it was natural for me to associate again and I found events of the past flooding back ever more easily and could retain in recent memory facts of the day more readily than at any time for seven years.

. . . Soon after this I realized that I could practice medicine again and in June 1952, announcements were sent to former patients and the physicians of the community informing them of my return to practice.

Now, a year and a half later, the confidence in my ability to carry on has not wavered. My fellow practitioners, with a few exceptions, were skeptical of my recovery and ability at fifty-seven years of age to pick up the continuity of work again. But as time passes, as former patients return and new ones enter my office to challenge my diagnostic skill and therapeutic ability, it is gratifying to be able to work again.

I still see Dr. Sakel once every week. My memory, in my opinion, is almost comparable to that of the average person of my years, but it does not yet compare to that marvelous memory I had before the electric shock treatments. Some of the ability I had then is returning. At times I meet a former patient or friend whom I have not seen for many years, and occasionally at once I know them and their name. At other times, these elude me temporarily to "come back to mind" hours later.

Memory of recent day to day events is still fleeting and requires me to keep minute notes of signs, symptoms and prescriptions for patients, but this I think will improve with training just as the recovery of past events back to childhood, university days and the years in World War I now much more easily are recalled in sequence with persons and places involved.

March 25, 1954

Important too is the therapeutic value of the insulin shock treatment without convulsions in manic-depressions in such cases where the episodes are frequent.

In adapting the Sakel Insulin Shock Treatment for depression, it is best to limit Phase I to as short a time as possible. The ascertaining of the shock dose should be confined to from ten days to two weeks. The smallest possible adjuvant convulsant to the insulin shock dose should be given as soon as possible to force the shock into a convulsion.

This careful and minutely considered handling should result in the complete clearing up of the depression with almost none of the side effects such as amnesia, temporary befuddlement or euphoria. Convulsion set by electricity will relieve the depressive episode just as effectively, but the side effects are unavoidable. The aggravation set up by these may result in a secondary reactive depression, which in some cases has led to suicide. The cumulative effect of too many convulsions may result in slight or severe permanent damage to the brain tissue, with a sequel of a total change in the personality of the patient suffering with a self-curative disease, such as depression.

In a manic condition, the situation is more difficult, and no definite treatment can be laid down as applicable to every case. Neither insulin hypoglycemia nor convulsions alone in the classical method are invariably effective. The only present procedure seems to be the utilization of the pacifying effect of the insulin borderline doses. This can be used in extreme cases up to three times a day. Hypoglycemia may be extended for such a period as seems desirable, but not longer than for four hours. It may sometimes be helpful to prolong the pacifying effect by application of protamine zinc insulin. This procedure may cut short the manic attack or reduce it to the mildest aggravation until the cyclic, fixed time of the episode has run its course.

In cases of manic episodes, this treatment has to be considered as symptomatic and palliative only. The pathologically exaggerated functioning of the nerve cells and disturbance of their directing hypothalamic centers of emotional response cannot yet be restored to normal function by a specific treatment.

The seat of the dysfunction seems to be the center low in the midbrain in the vicinity of the other periodic centers which direct the cycle of life: for example, sleep, etc.

For therapeutic purposes, it is necessary to mention the difficulty in distinguishing between a manic depression and a neurotic depression. This is of vital importance since the treatments are totally different. In a neurotic depression, convulsions are of less than no therapeutic value. In the majority of cases, they are aggravating.

To repeat, in neurotic depressions, slow but satisfactory results are obtained by a systematic application of the borderline insulin dose treatment which strengthens the structure and reserve energy and reinforces the action capacity of the nerve cell. This treatment must be accompanied by competent psychotherapy.

Lack of space and time compel me to omit dealing in this paper with the indications and results of lobotomies and topectomies, but I have to mention them because I have to deal with their aftereffects. It can be stated that these are not *treatments* for any disease. Rather they are amputations and, therefore, may produce unsatisfactory end results which need treatment in turn. They should only be resorted to in a case where the best available treatment has proved unsuccessful. We have not progressed so far in psychiatry as to be able to operate on the brain with infallible precision, since the location of the various functions of mental and emotional processes cannot yet be pinpointed in normal brains—much less in psychotic ones.

This being the case, it has been found impossible to restore, even to tolerable functioning, many psychiatric cases (schizophrenia and other mental diseases) upon which lobotomies or topectomies were performed. There may be two reasons for this: (1) The basic psychotic process was inaccessible to the influence of the operation and therefore the expected result —the retarding or diminishing of the emotional reaction was not achieved. (2) The operation may have caused an additional damage and thus may have aggravated the previous psychotic one.

In many cases of brain operations in which the results did not even succeed in ameliorating the patient's condition, I observed that a very prolonged insulin borderline treatment with shock phase interjections proved beneficial. The process can be compared to the results obtained with patients who were suffering from the aftereffects of too many convulsions, that is with partial, organic, brain damage. The borderline insulin treatment seems to activate a great number of dormant reserve brain cells undamaged by the operation (or the convulsion) and making them substitute for those damaged or destroyed by the operation. The shocks interjected in this procedure helped to diminish the basic psychotic process, which had remained unaffected by the operation. This postoperation treatment should be extended according to my recent experience over a period of about a year. In such cases great care must be exercised in determining the exact procedure and in deciding

when the activation of the reserve undamaged cells is more important and when the shock treatment is preferable in order to influence and subdue the psychotic process.

In cases of other marginal psychiatric nervous-emotional conditions, the beneficial application of different variations of single factors of the insulin hypoglycemic treatment whether by themselves or combined with psychotherapy is not yet fully explored.

Different personality types manifesting themselves in various degrees of mental or emotional weakness or strength may be expressing an organic underdevelopment of the central nervous system and its inability to cope with normal situations. Even the human faculty of abstract thinking and concepts of fundamentals such as justice, etc., are the normal, though highly advanced, functions of the basic mechanisms of this system. Inadequacy of these mechanisms, whether constitutional or acquired will reveal itself in the lack of such fundamental concepts.

In some *diseases* of the central nervous system, such as schizophrenia or cyclothemia, we come much nearer to an understanding of their pathobiophysiological mechanisms through their response to some physiological factors of the Classical Insulin Shock Treatment.

On the other hand, neuroses, psychopathic reactions, and other marginal psychiatric groups are still far from being understood in their relation to some underlying central nervous mechanism. A physiological explanation for these conditions has not yet been found. We can only assume a weakening in the functions of the central nervous system or a depletion caused by some "outer" psychological or "inner" physiological trauma. Even if the psychological explanation were an established fact, it would not necessarily preclude the possibility of the curative factor of strengthening the central nervous system by medico-physiological means.

The purely psychological explanation of neuroses seems insufficient in view of the meager success achieved in attempts to treat neurotics in this way, nor is the great prominence given in literature to psychoanalytical speculation on this subject justified by therapeutic results.

When dealing with patients, it is the concrete results that have to be observed, and for that reason, it is significant that the use of insulin borderline doses in neuroses has achieved successful results where the doctrinal procedure had failed. I am including a brief outline of a treatment for this psychiatric peripheral condition (which I have developed further but not published), because the number of neurotic patients is incomparably greater than the number of seriously mentally sick, and neurotics should not be denied medical help.

Psychotherapy cannot be omitted because it is essential in eradicating undesirable conditioned reflexes and in forming new thought patterns.

The mechanism of neurosis is not fully understood, since we cannot yet say with finality that we have grasped the mechanism of normal emotional action and response. The problem of neurosis is therefore hardly touched as far as scientific knowledge of its cause is concerned. Each case has to be considered individually and the various treatments, physiological and psychological, carefully scrutinized before using them. No factor or branch of knowledge can be discarded as of no value.

It can be definitely said that in cases where psychoanalysis is adopted as the treatment of

choice, small doses of insulin support even this procedure by their pacifying and restorative effect. Even if the physiological advantage should be small, the psychological one can be great by giving the patient the assurance that something more concrete than discussion is being done for him. The improvement appears to take place by improving the resilience and resistance of the nerve cells, forcing them through hypoglycemia to replenish their depleted reserves. The nervous structure thus functions with less effort and allows surplus energy for the restoration of the nerve cells and an ultimate resumption of normal, unrestrained functioning.

The results are not definite in all cases of neurosis as they can be claimed in psychotic conditions, but they are definitely better than in cases of neurosis treated only psychologically.

To strengthen this conclusion, conservative though it is, I would like to report that I have successfully treated many cases which had been treated for years by psychoanalysis without any improvement at all. After the Borderline Insulin Treatment, they recovered to a point beyond their previous limited, "normal" functioning. For example, one case was not able to leave the apartment for fear of failure, and if left in company, even with the doctor, got into an extreme panic if he set foot outside his home. He has now been completely well for a number of years. In this case, daily varying doses were administered of not more than from 10 to 40 units of protamine zinc insulin. The treatment was combined with psychotherapy. Together they achieved a successful result.

In conclusion, I would like to review the present attitude to the problem of the mentally diseased and to suggest a few propositions which could serve as a guide for those who wish to help with the work of solving this problem.

One of the most striking sociological features of modern society is its concern shown for its mentally and emotionally disturbed members. Not very long ago, these unfortunates were the almost forgotten and decidedly neglected step-children of the medical profession. Today the general public is conscious of its responsibility towards these helpless and afflicted people. A sense of the urgency of their need, together with a genuine desire to alleviate their suffering, has replaced the neglect that was doubtlessly born of the feeling of impotence and utter frustration in dealing successfully with the most baffling of human diseases.

This unity of purpose in solving the problems in the spheres of emotional and mental diseases could be very valuable were it not for the fact that anything, if overdone, can lead to exactly the opposite of the desired effect and thereby vitiate the progress made thus far. I wish, therefore, to call attention to two danger points which threaten to damage the advances made in the medical science of psychiatry and to bring harm rather than healing to the genuine hospitalized psychiatric patient.

The first danger stems from the public preoccupation with abstract popular psychiatry. Under the influence of the volume of accessible psychiatric literature, widespread familiarity with catch-words, ill-defined scientific psychological and medical problems and ill-formulated theories may push us from the narrow path of scientific therapeutic experiment, which must always be bounded by practical results. The alternative path is that of scholasticism, which, however brilliant it appears, may serve to conceal the absence of a true scientific approach or the lack of therapeutic results. This is perhaps because such literature appeals to those

who are seeking a solution to their social or environmental conditions but who are not actually incapacitated through disease. The natural interest in a sheer bulk of psychiatric literature already threatens to detour medical psychiatry into exploring only the possibilities of consoling "couchside manners" within a philosophic, dialectic framework in its search for answers to what are strictly *medical* problems. This does not mean that psychotherapy is not important. The knowledge of the psychology of individuals, of the intersocial relationships among people, as well as of the formations of psychological attitudes and behavior patterns in sociological groups, is most important in the consideration of the particular diagnosis and treatment for every type of mental and emotional disease. But though it is a vital aspect to write about and a fascinating one to read, it is only one aspect of a complex phenomenon.

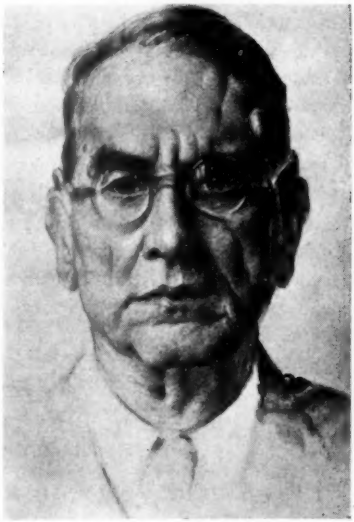
It must be pointed out that out of 10 patients discussed in popular or scientific literature, only 1 is a real medical hospital problem. The other 9 are justified in having sympathetic psychotherapeutic or "couchside manner" help—for that matter, every patient needs it—but the exclusive preoccupation with this approach threatens to put all psychiatric patients in one single category to be treated by one single method. This attitude can be compared to treating a cancer patient with aspirin, because it has a helpful effect on headcolds. It has led to a dangerously deceptive result in that psychiatry is considered to be successful because it claims the cure of the nine so-called patients. The statistics do not reveal the stark fact that these "patients" could have been cured equally well by means of moral support or even without it, while the one genuine patient remains hopelessly sick and condemned to a lifetime in a hospital. The real problem of psychiatry is this one patient, whom, through lack of the requisite knowledge and skill, the doctors cannot cure. This patient and those like him are the ones who should be the central preoccupation of all those concerned with psychiatry. They are the true challenge to medicine and science and are the tragic burden which weighs down the economy of the nation.

The failure to recognize this basic fact has led to the widespread belief that mental and emotional illnesses, rather than differing in kind, differ only in degree. This in turn has been responsible to a large extent for the failure to deal with the hard core problem of psychiatry. Eighty per cent of hospitalized psychiatric patients are schizophrenics. A more precise evaluation of the number of so-called "cures" would leave the record of positive achievement with those considered of unsound mind, an almost complete blank. It is not only unscientific, but highly unjust to continue in the current practice of judging all categories of the mentally and emotionally disturbed as if they were different in degree only and of treating them all almost solely with some kind of verbal therapy.

It is astonishing that what should appear so obvious to anyone who really wishes to ascertain the correct facts for himself has not led to a critical examination of the theories and doctrines on the causes of mental and emotional disease. The fascination and literary perfection of these writings, which concern and which appeal to the wealthy and perfectly competent patient, successfully obscure the urgent problem of the voiceless, disenfranchised, imprisoned poorest of the poor, those helpless, pathetic patients who, hidden away in our mental institutions, are denied their own and society's protection. They are not being

helped, because we are blinded by our belief in uncritically accepted theories and accustomed to the use of ineffectual treatments. This constitutes the first great danger to successful progress in psychiatry.

The second danger lies wholly within the realm of scientific medical practice. It has been elucidated fully in this paper. So that there can be no misunderstanding, however, I will restate it.



PROF. POETZL

Briefly, a proven, therapeutically valuable avenue of psychiatric therapy for a hitherto incurable disease has been blocked and left virtually neglected. The reason for this is that the basic clinical procedures by which, as I showed 27 years ago, I was able to influence mental and emotional disorders and to achieve therapeutically beneficial results have become so mechanized that they have led and are leading to a rigid and technicological push-button application of a treatment which, to be properly administered, must be flexible and individualized. The disrepute into which the routinized use of shocks has fallen is entirely deserved. It does not discredit the value of the Classical Sakel Insulin Shock Treatment from which it derived but only discredits the false reasoning which isolated one single factor, the convulsion, out of its context in the shock treatment as a whole and elevated it to the unmerited position of constituting the whole treatment. This process, which amounts in some cases, to put it mildly, to the neglect of the patient, is unwarranted in all but a few conditions of depressive melancholia.

This lamentable process was partly caused by the confusion created by the loose use of the term "shock" to cover a variety of techniques: "shock" was the original term created by Dr. Sakel for the total "Sakel treatment," which embraced convulsions, now identified as shocks as well as comas. The original Sakel Insulin Treatment consisted of more factors than a convulsion, presently called shock. The term "shock treatment" has passed into common usage as meaning exactly what it says: a treatment which consists of administering a shock to a patient. Since metrazol shock is seldom used any more, the shock is commonly thought of as being electrically induced. It might be helpful to reserve the word "shock" in future medical literature with a designation only, for example, electrical shock, etc. It would be clarifying to use the term "Sakel treatment" in order to identify it as the original classical insulin shock treatment. By doing so there would no longer be any possibility of confusing the part factors of the Sakel treatment with the whole classical treatment as such. Moreover this would also prevent the perfunctory application of insulin by the inexperienced physician from being accepted as a well-administered treatment.

The distortion of the "Sakel" method has come into such widespread use that its unsatis-

factory therapeutic results unfortunately seem to have obscured the valuable possibilities inherent in the original technique. Many of the younger generation of physicians have never had the opportunity to learn even the *elements* of the whole Sakel classical insulin treatment. If better training in the intricacies of the Sakel insulin treatment in all its variations were available, it might well lead to a better record of success in the task of helping the mentally and emotionally afflicted. The plea I submit on behalf of these human beings is not for more psychiatrists but for *more adequately trained ones*. If it were answered, it would be possible to achieve the mastery of a treatment which would eventually have the result of diminishing the number of inmates in our overfilled mental hospitals and of allowing many of them to return to a normal existence in society.

The credit and the sole merit for the acceptance in our time of the physical therapies for psychiatric diseases that I introduced is owed to Prof. Poetzl, who had the greatness not only to understand my concept but to put it to work immediately in 1933 after becoming acquainted with it, and he also had the unequivocal courage and selflessness to turn over his psychiatric division of the Vienna Medical School to my discretion to apply in each case I deemed suitable, without being outranked, the treatment I introduced. Thus, it was greatly through Professor Poetzl that psychiatry was brought back into the fold of scientific medicine, instead of remaining idle speculation. Professor Poetzl did this for Science only: he consistently refused to take any credit for the part he played through his belief in the Classical Sakel Insulin Shock Treatment. He stated ". . . what I did was my obligation to Science, but I didn't contribute to your [Sakel's] work—just to Science."

BIBLIOGRAPHY

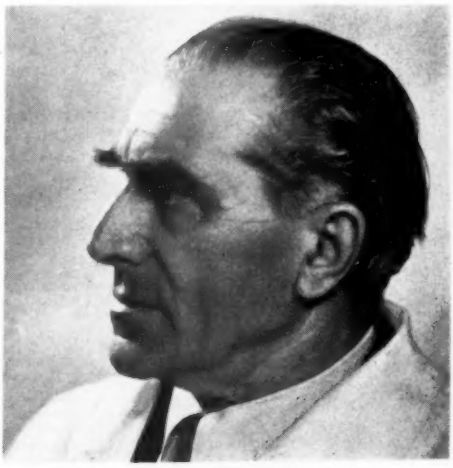
1. Neue Behandlung der Sucht, 1928.
2. B. M. W. Neue Behandlung der Schizophrenie, Sept. 5, 1933.
3. Wiener Medizinishe Wochenschrift. 1933-1934.
4. Schock Behandlung der Schizophrenie, 1935. (Perles.)
5. VON MEDUNA: Convulsive Therapy of Schizophrenia, 1939.

Biographical Note

UGO CERLETTI

Ugo Cerletti, professor of Neuropathology and Psychiatry at the University of Rome, is also director of the Center for the Study of the Physiopathology of Electroshock (founded by the National Research Council), continuing research on electroshock therapy, originally presented by him in 1938.

Doctor Cerletti was born at Conegliano, Italy on September 26, 1877. He studied medicine at Rome and Turin, and later did extensive work in neuropsychiatry at Paris, Heidelberg and Mûnich. During the first World War he served as a volunteer in an assault company in the Alps, and in 1916 patented a delayed action fuse, which was adopted by the Italian army.



UGO CERLETTI

After this war Dr. Cerletti became director of the Neurobiologic Institute of the Milan Mental Diseases Hospital (later the Institute for Researches in Psychiatry). In 1924 he was appointed director of neuropsychiatry at the new University of Bari, where he founded an outpatient clinic. Four years later, appointed professor of neuropsychiatry at Genoa, he directed construction of the modern neuropsychiatric clinic there, still one of the finest in Italy. In 1935 Dr. Cerletti was appointed to the University of Rome.

Doctor Cerletti is president of the Società Italiana di Psichiatria, member of the board of directors of the Società Italiana di Neurologia, the Società Internazionale di Criminologia, the Accademia Lancisiana, the Deutsche Kaiserliche Leopoldine Kuralinsche Akademie, and the Société Suisse de Psychiatrie, and honorary member of the Electroshock Research Association, the American Neurological Association, and the Société Française de Neurologie.

At present Dr. Cerletti is directing research for the prevention of goiter in his country, is experimenting with electroshock in animals, and is also actively engaged in studies in prehistory.

Biographical Note

JOSEPH L. MEDUNA

Joseph Ladislas Meduna has continued his work in the development of Metrazol convulsive treatment of nervous and mental disorders since his arrival in this country in 1939, and lately has devoted his attention to the application of carbon dioxide therapy to the treatment of neuroses. He is now professor of psychiatry at the University of Illinois Neuropsychiatric Institute School of Medicine.

Doctor Meduna was born in Budapest, Hungary on May 27, 1896. He received his medical degree from the Royal University of Sciences, Budapest, in 1921. From 1924 to 1927 Dr. Meduna was assistant professor at the Budapest Interacademic Institute for Neurological Research, and from 1927 to 1933, associate professor at the Department of Psychiatry at the Royal University of Sciences, University Clinic for Mental and Nervous Diseases. From 1933 to 1939 he was also medical director of the male ward of the Leopold Field Hospital in Budapest.

JOSEPH L. MEDUNA

For the next four years Dr. Meduna was associate professor of psychiatry and neurology at Loyola University in Chicago. Since then he has been at the University of Illinois.

Doctor Meduna was married in 1934 and became a citizen of the United States in 1944—"The two most important dates in my life."

Doctor Meduna is an honorary member of the Sociedade de Medicina de Pernambuco, Brazil, a corresponding member of the Associaçao Paulista, member of the Hungarian Neurological Society, the Hungarian Psychiatric Association, the Chicago Neurological Society, the Electroshock Research Association, the American Psychiatric Association, the New York Academy of Science, the American Medical Association, the Central Neuropsychiatric Association, Phi Beta Pi, and Sigma Xi.

Biographical Note

MANFRED J. SAKEL

Manfred Joshua Sakel came to the United States in 1936 and was asked by the Commissioner of Mental Hygiene of the State of New York to teach 40 American physicians in a six week full-time course his already Europe-acknowledged successful approach of treating nervous and mental diseases by medical means, then called shock treatment. Doctor Sakel accepted this request and taught the 40 physicians, who were from all over the United States and Canada and who were primarily staff physicians of mental hospitals, the use of the shock treatment.

Born in Nadvorna, Austria on June 6, 1900, he is a direct lineal descendant of Maimonides, the twelfth century physician and philosopher. Doctor Sakel is the third person of his ancient family to take up the study of medicine, bridging a gap of 700 years. He studied at the First State College of Brno, Czechoslovakia, and at the Medical School of the University of Vienna, from which he received his medical degree in 1925.

For two years Dr. Sakel was associate physician at Vienna Hospital. In 1927 he was appointed research fellow at Urban Hospital in Berlin and that same year became psychiatrist in chief of Lichterfeld Hospital, also in Berlin. From 1933 until he came to the United States three years later, Dr. Sakel was an associate in the Neuropsychiatric University Clinic in Vienna.

MANFRED J. SAKEL

Clinical evaluation in the United States of insulin shock therapy was carried out by Dr. Sakel himself at the Harlem Valley State Hospital, which was selected by the Commissioner of Mental Hygiene for that purpose, and which was under the superintendentship of Dr. John D. Ross.

Throughout the years of his contact with nervous and mental patients and his concomitant research, Dr. Sakel became convinced that the problems of mental disorders must be approached by medical means as well as psychological. He was governed by his conviction, gathered from his clinical experience, that mental and emotional disturbances are illnesses of the total human being, and could not be diseases of an abstract concept called the mind. "Being a physician," he has said, "the concept of oneness made me unable, even in considering psychiatric problems, to think of mental manifestations as anything other than phenomena of the whole, living human being."

Since 1936 Dr. Sakel has practiced psychiatry privately in New York City. He is medical director of the Manfred Sakel Research Foundation, and a Fellow of the American Psychiatric Association.

Doctor Sakel is the author of a number of books and papers on psychiatric problems, particularly those concerning therapies such as shock treatment, among them: Theory of Addiction; New Treatment of Addiction (Morphinism, Alcoholism); New Method of Treating Nervous and Mental Ailments, The Pharmacological Shock Treatment of Mental Diseases; The Result of Shock Therapy; The History of the Origin of Shock Therapy; Medical Psychiatry and Psychological Medicine; An Approach to the Causative Treatment of Idiopathic Epilepsy.

QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

*

Incorporating the International Record of Psychiatry and Neurology

WINFRED OVERHOLSER, M.D., editor-in-chief

Professor of Psychiatry, George Washington University School of Medicine
Superintendent of St. Elizabeths Hospital

national editorial board

SPAFFORD ACKERLY, M.D.
Professor of Psychiatry,
University of Louisville Medical School

A. E. BENNETT, M.D.
Associate Clinical Professor of Psychiatry,
University of California Medical School

KARL M. BOWMAN, M.D.
Professor of Psychiatry,
University of California Medical School

FREDERIC A. GIBBS, M.D.
Associate Professor of Psychiatry,
Illinois Neuropsychiatric Institute

EDWARD J. HUMPHREYS, M.D.
Assistant Superintendent,
Norristown State Hospital
Norristown, Pa.

SOLOMON KATZENELBOGEN, M.D.
Clinical Professor of Psychiatry
George Washington University
School of Medicine

WILLIAM MALAMUD, M.D.
Professor of Psychiatry,
Boston University School of Medicine

J. M. NIELSEN, M.D.
Associate Professor of Neurology and
Psychiatry, University of Southern California

LEWIS J. POLLOCK, M.D.
Professor of Neurology,
Northwestern University Medical School

TRACY J. PUTNAM, M.D.
Professor of Neurology, College of
Physicians and Surgeons, Columbia University

MORTON A. SEIDENFELD, PH.D.
Director of Psychological Services,
National Foundation for Infantile
Paralysis, Inc.

LAUREN H. SMITH, M.D.
Professor of Psychiatry,
University of Pennsylvania

JOHN C. WHITEHORN, M.D.
Professor of Psychiatry,
Johns Hopkins University Medical School

international board

MACDONALD CRITCHLEY, M.D.

Physician, National Hospital
Queen Square, London

MOGENS ELLERMAN, M.D.

Assistant Director, Sct. Hans Hospital
Roskilde, Denmark

HENRI EY

1, Rue Cabanis
Paris (XIVe), France

HANS HOFF, M.D.

Professor, Neurology and Psychiatry,
University of Vienna
Vienna, Austria

GONZALO R. LAFORA, M.D.

Director, Psychiatric Clinic for Men,
General Hospital of Madrid;
Associate Professor of Psychiatry and Neurology,
Madrid Medical Faculty
Madrid, Spain

EMILIO MIRA Y LOPEZ, M.D.

Former Professor of Psychiatry,
University of Barcelona;
Professor of Normal and Abnormal Psychology,
Getulio Vargas Foundation, Rio de Janiero
Rio de Janeiro, Brazil

G. H. MONRAD-KROHN, M.D., F.R.C.P. (Lond.)

Professor of Medicine
University of Oslo
Oslo, Norway

ABRAHAM MOSOVICH, M.D.

Research Associate in Neurology
Instituto Experimental del Cancer;
Chief in Electroencephalography,
Department of Psychiatry,
Medical School of Buenos Aires

F. D. ROEDER, M.D.

Professor of Neurology and Psychiatry,
University of Göttingen
Göttingen, Germany

J. O. TRELLES, M.D.

Professor of Neurology,
San Marcos Univ. School of Medicine
Lima, Peru

ERIC WITTKOWER, M.D.

Assistant Professor of Psychiatry,
McGill University
Montreal, Canada

JAKOB WYRSCH, a.o.

Professor of Psychiatry,
University of Bern
Bern, Switzerland

INCORPORATING INTERNATIONAL RECORD OF PSYCHIATRY AND NEUROLOGY

FOREWORD

The purpose of the QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY is to present promptly brief abstracts, noncritical in character, of the more significant articles in the periodical medical literature of Europe and the Americas.

For readier reference, the abstracts are classified under the following general headings:

PSYCHIATRY

1. Administrative Psychiatry and Legal Aspects of Psychiatry
2. Alcoholism and Drug Addiction
3. Biochemical, Endocrinologic and Metabolic Aspects
4. Clinical Psychiatry
5. Geriatrics
6. Heredity, Eugenics and Constitution
7. Industrial Psychiatry
8. Psychiatry of Childhood
9. Psychiatry and General Medicine
10. Psychiatric Nursing, Social Work and Mental Hygiene
11. Psychoanalysis
12. Psychologic Methods
13. Psychopathology
14. Treatment
    a. *General Psychiatric Therapy*
    b. *Drug Therapies*
    c. *Psychotherapy*
    d. *The "Shock" Therapies*

NEUROLOGY

1. Clinical Neurology
2. Anatomy and Physiology of the Nervous System
3. Cerebrospinal Fluid
4. Convulsive Disorders
5. Degenerative Diseases of the Nervous System
6. Diseases and Injuries of the Spinal Cord and Peripheral Nerves
7. Electroencephalography
8. Head Injuries
9. Infectious and Toxic Diseases of the Nervous System
10. Intracranial Tumors
11. Neuropathology
12. Neuroradiology
13. Syphilis of the Nervous System
14. Treatment
15. Book Reviews
16. Notes and Announcements

In fields which are developing as rapidly as are psychiatry and neurology, it is obviously impossible to abstract *all* the articles published—nor would that be desirable, since some of them are of very limited interest or ephemeral in character. The Editorial Board endeavors to select those which appear to make a substantial contribution to psychiatric and neurologic knowledge and which promise to be of some general interest to the readers of the REVIEW. Some articles, highly specialized in character, or concerning a subject already dealt with in an abstract, may be referred to by title only at the end of the respective sections.

A section entitled INTERNATIONAL RECORD OF PSYCHIATRY AND NEUROLOGY is included at the beginning of the journal. The Record Section consists of advanced clinical and experimental reports.

The Psychiatry and Neurology Newsletter was compiled by Doctors Leon Epstein and Francis N. Waldrop.

The Editorial Board at all times welcomes the suggestions and criticisms of the readers of the REVIEW.

WINFRED OVERHOLSER, M.D.
Editor-in-Chief

Psychiatry and Neurology

NEWSLETTER

PSYCHOTHERAPY CHANGES EVALUATED: A battery of seven tests was administered to patients of the Kaiser Foundation Psychiatric Clinic, Oakland, California, with the aim of obtaining more precise personality measurements in order to evaluate changes resulting from psychotherapy. Three groups were tested: 127 persons receiving group psychotherapy, 67 receiving individual psychotherapy, and 84 who were tested before and after a waiting period of several months during which no treatment was administered. Doctors Leary, Powelson, and Sarvis of the Kaiser Foundation Hospital staff and Dr. Coffey of the University of California will present their conclusions in a book in the near future.

LOUISIANA HEALTH REPORTS: A Way Out, the report of the Survey and Planning Committee on Mental Health Needs for Louisiana, is available from the Department of Institutions, Baton Rouge, Louisiana. This planning committee studied the institutions as well as the mental health problems in that State, and this report represents a condensation of their findings.

CLASSIFICATION FOR CASE HISTORIES: John Dollard, Yale University, reports that he is "trying to devise a reliable system of categorizing the sentences or independent clauses in a psychotherapy case record. . . . The problem is to find a useful category system for these units. If such a system can be devised a further problem would appear--namely, how the sentence counts for particular categories are interrelated. The inciting dream of the research is that such a category system might make it possible to compare, for instance, different phases of a therapy case or different series of initial hours in a different case."

STUDIES ON CATASTROPHIC EXPERIENCES: David P. Boder, University of California, is conducting a series of 4 studies on the assessment and evaluation of catastrophic experiences. The first study deals with the content analyses and traumatic evaluations of wire recorded interviews from a collection obtained in displaced persons camps and shelter houses of Europe during the summer of 1946. Another study is devoted to analysis of interviews obtained from sufferers of the Kansas City flood in 1951 with broad bases of comparison of traumatizations inflicted by a nature-made disaster in a friendly and intact environment versus man-made catastrophe in a hostile environment. The first of these studies appears in the current issue of "The Journal of Psychology."

CANADIAN RESEARCH IN SCHIZOPHRENIA: Investigations are being conducted in Canada relative to certain biochemical, endocrinologic, and metabolic aspects of schizophrenia. F. Dequin of the Saint-Jean-de-Dieu Hospital at Montreal is studying intermediary nucleoprotein metabolism in schizophrenics. G. E. Bobbs of the University of Western Ontario is investigating the acute reactivity of the adrenocortical system in schizophrenics and the value of this index in the diagnosis and prognosis of the disease. Lovett Doust of the University of Toronto is currently working on estimates of fetal hemoglobin in a group of these patients. Stefaniuk of Saskatchewan Hospital is evaluating nucleotide therapy in a group of 40 schizophrenic patients.

SOCIAL FACTORS AND MENTAL ILLNESS: At Yale University investigations are in progress on the relationship of social factors to mental illness. The results of these investigations will be presented in two volumes. The first by Hollingshead and Redlich will deal with psychiatric treatment in relation to social stratification, and the second by Roberts and Myers will be focused upon the family structure, social stratification, and mental illness.

BEHAVIOR CHANGES: Carl A. Pribram, Institute of Living, Hartford, Connecticut, is investigating changes in primate behavior following surgical procedures on the temporal lobes in an effort to define and fractionate the "temporal lobe syndrome." This work involves surgical interference with neuronographically determined areas rather than with anatomic areas as defined by older technics.

PSYCHOLOGIC AID: A manual, Psychological First Aid in Community Disasters, has been prepared by the Committee on Civil Defense of the American Psychological Association. It is available to individuals and groups who may be called upon to help care for emotionally disturbed victims of community catastrophes and briefly outlines certain ways they can give psychologic first aid. Disaster workers are advised to (1) accept every person's rights to have his own feelings, (2) accept a casualty's limitations as real, (3) size up a casualty's potentialities as accurately and as quickly as possible, and (4) accept their own limitations in their relief roles. A section is also devoted to caution about the use of drugs. Copies of this pamphlet may be obtained from the American Psychiatric Association, 1785 Massachusetts Avenue, N. W., Washington, D. C.

QUARTERLY REVIEW OF PSYCHIATRY AND NEUROLOGY

Incorporating the International Record of Psychiatry and Neurology

Countertransference: Its Influence On A Patient's Capacity for Awareness*

Daniel S. Jaffe, M.D.

WASHINGTON, D. C.

In the past few years there has been a marked growth of interest in the problems of countertransference. A number of comprehensive reports have recently been published,[1-11] dealing with the manifestations and implications for therapy of the *analyst's* emotional contributions to the treatment process.

The present report is an attempt to describe an interaction in which a patient's solution of certain problems occurred only after the attitudes of the therapist had undergone modification, all outside of awareness at the time. The clue, in a retrospective evaluation of the treatment in this case, hinges on the appearance of the analyst as himself in the first dreams reported by the patient. This phenomenon is dealt with in a recent paper by Gitelson,[8] and the conclusions arrived at there will be briefly summarized now, as background for the understanding of our present case.

In considering the effects of the analyst's reactions, Gitelson states a viewpoint shared by other writers on the subject, namely, "no analyst enters upon the analysis of another person without residual potentialities for reaction either to the patient, the patient's material, the patient's transferences, or the patient's real attitudes toward him as a real person. These potentialities belong to the fact, as Freud has shown, that analysis is interminable. They are the result of presentations by the patient which touch on surviving transference potentials or on still vulnerable aspects of the analyst's narcissism and character defenses."[8]

---

* Read at the 17th annual meeting of the Medical Society of Saint Elizabeths Hospital, Washington, D. C., April 23-24, 1954.

Further, as stated by Glover, ". . . a 'third ear,' directed toward himself, maintains the continuing prospect of resolving the analyst's own interfering emotions while coping with those of his patient. This perhaps, is the most important technical qualification of the analyst."[12]

As an indication that the analyst's reaction may be reflected in the patient's dreams, Gitelson stated that "an unmanageably intense transference neurosis is likely to be heralded in the patient's first dreams by the appearance in them of the analyst as himself. Such dreams are indicative of the actual recurrence in the analytic situation of an emotional situation which is too nearly like that which characterized an original relationship, and the analyst needs to be certain that it is not his own attitude towards the patient which is producing the reaction."[8]

In contrast to this initial dream phenomenon, it is further stated that dreams later in treatment, in which the analyst appears as himself, can be capitalized on in the interest of the patient if both sides of the equation are analyzed. That is, if the analyst is open enough to analyze his own contribution, this helps clarify the patient's transference.

However, it is assumed that the extent of the problem in the analyst, when the latter appears in the patient's initial dreams, may preclude resolution and even constitute an indication for discontinuation of treatment with that analyst.

A case is cited by Gitelson in which, at the beginning of treatment, the analyst reacted to a patient's self disparagement by reassuring her with a statement that *he* had a good impression of her. The next hour, the patient came in with a dream in which the analyst sits before her with his penis exposed but flaccid. The patient then broke off treatment during the trial period. The interpretation of the countertransference operation involved was to the effect that the "therapeutic kindness" represented the analyst's abiding need to reduce the intensity of his own unresolved sado-masochistic impulses.

This example is cited because of the similarity of the operations and of their implications, with the case to be described here.

Our patient was a 28 year old unmarried white female of high intellectual capacity, who sought treatment because of an intensification of a number of phobias, as well as for a lifelong problem of stuttering. During the first two interviews, the details of her current situation and some of her earlier background were given. In the third hour, the following dream was reported:

> It was the end of our hour today. I was standing up to leave. I said to you, "I'll see you at 12 tomorrow then." You said, "I can't see you tomorrow because I have a luncheon at the Psychoanalytic Society." I felt disappointed. Then you said, "this same situation will probably come up from time to time but I'll try to work it out so the same patients don't have to miss appointments each time."

In association to this dream the patient stated that she was worried about missing appointments, would be disappointed in such a situation, and would want reassurance. She noted that in having gone into detail in explaining her stuttering reactions, she had actually been asking for reassurance, and that in the dream, she felt, she had gotten it. She then stated, "I am apt to analyze someone's reactions to me and to reinterpret even their most

innocuous remarks." It was then developed that she did find it difficult to believe that others really accepted her, even when they so professed.

It is quite clear from this material that the patient had misgivings about my ability to accept her. Looking back at the first interview, it is noted that in it she had described a meeting with another psychiatrist who had expressed doubts about his ability to be objective in dealing with her stuttering. At the end of our first hour, she had asked whether I had any problem in dealing with stuttering, or if I had been uncomfortable with it that hour, and I had replied that I had not. That the dream and its associations were referring to this, seems unmistakeable. However, I believe that the patient was communicating something more than simply that my statement professing acceptance was evidence of a defensive operation. If we recall her words, "I am apt to analyze someone's *reactions* to me and to reinterpret even their most innocuous remarks," we may suspect that she was perceiving something operating on a *nonverbal* level, as countertransference. Rather than attempt to describe what this may have consisted of at the time, it may suffice to note the subsequent course of events and to find a correlation between the anxiety potential of the patient and my own. First, a brief summary of the patient's early significant relationships and of her character structure may help in understanding the interaction.

The patient was the first of three children, and the only girl. There were two siblings, one a brother, two years younger, who had died of diphtheria when the patient was about 7 years old, and the other, a brother eight years younger. Her attitude towards her brothers had always been an affectionate one in many ways but with strong elements of envy and competition, and she had taken pleasure in dominating and provoking them. She had suffered strong guilt feelings at the death of the first brother on this account. Of all the children, she had been told, she was the easiest to rear, yet she had often had periods when she was irritable and intractable. Her stuttering had started at about the age of 6. The brothers had been more overtly disturbed and had presented problems of feeding and toilet training, with bed-wetting, temper tantrums, head banging, and negativism.

Both parents were described as tense people. The father worried a great deal, suffered from "nervous indigestion," and was a man of "quick temper." By the same token, he was quite open in his expressions of affectionate feeling, and in the patient's eyes, especially in later years, he was more accepting and understanding than was her mother. The latter never brought her feelings of aggression into the open. She tended to martyr herself, to look for slights by other people, and to present a moralistic or self-righteous attitude. She had frequent "sick headaches," and cried easily. This was her usual reaction in family arguments, instead of fighting back. She often did without things for herself when it wasn't necessary to do so, and on the whole, she set up for herself and for the patient a distorted and idealized standard of what a person should try to be. Yet, at the same time, the patient sensed in her mother a certain attitude toward allusions to punishment or harshness, resembling that of suppressed glee. Both parents were outgoing people, mixed readily, had a wide circle of friends, and were active in social and community affairs.

The patient's character structure may be viewed primarily in light of the apparent extent of the sado-masochistic problems described in the mother. The patient's demeanor conveyed

a certain intensity but with a feeling of something always being suppressed, held back. An overriding need to be right seemed to interfere with spontaneous freedom of attitude or action. Thus, despite a great deal of native ability, there was constant doubt about the acceptability of her work or of herself personally. Indecision and undoing were prominent characteristics. A marked degree of envy and competitiveness were balanced by a strong need to appease, to bend over backward to acquiesce. Intense drives to have what she wanted were constantly getting checked by equally prominent manifestations of self-censoring and reparative efforts. Thus, masochistic fantasies constituted an important part of the patient's inner world from early life, and by assuming the position of the sufferer, the energy of the aggressive impulses were drained off by being turned against the self. In her relationships with others, however, the competitiveness and castrative attitudes were a constant source of disruption. In respect to the predominant symptom of stuttering, it was clear that this represented, as in the view of Coriat,[13] a problem of fixation at the oral level as a defense against the threat of castration or destruction; with repression of the oral-sadistic affect producing the anxiety lest the impulses be revealed. The phobias were an expression of this anxiety as the underlying impulses approached awareness.

In sum, a severe limitation of awareness of aggressive impulses had been imposed on this patient through maternal anxiety and therefore prohibition in this area, and at the same time, a motivational structure including these impulses remained central in the patient's living.

In light of this background, it seems likely that the patient would tend to provoke and yet would be on the alert for, and react adversely to, any manifestations in another person of the suppressed tendencies or of the character defenses she had encountered in the mother. These would include any shadings of sado-masochistic conflict, such as coercive, demanding, competitive, aggressive, self-centered trends; or of apologetic, obsequious, self-effacing attitudes; or of both. That the evidence from the initial dream pointed to the patient's sensitivity to such capacities in myself, is clear, in retrospect, though at the time I was aware neither of the presence of such operations, nor of the significance of the early dreams as tokens of them. The awareness of these repressed tendencies came about in the course of my own analysis, which was proceeding concurrently. As an expansion of awareness of these aspects of self occurred, we began to hear more deep-seated material from the patient dealing with these problems in herself, presumably as evidences of my anxiety in touching on them diminished. From a rigid, rehearsed type of production in the treatment situation, as well as in her dealings with others outside, the patient began to show a greater latitude in self expression. With this, the phobias cleared up; and in a more gradual way, as deeper levels were worked through, there was an amelioration of the more basic difficulties, such as the stuttering and character defenses, evidenced in an improvement in the nature of her relationships with others.

It is probable that this movement hinged on sufficient freedom from anxiety in the transference-countertransference interaction to permit the dissociated material to come up for recognition and working through.

As a conclusion from this, we can see the importance of becoming alerted to evidences of

countertransference operation through the many clues we are learning to use to warn of it. (Dr. Mabel Cohen in her article on countertransference,[9] lists a great many additional signals of countertransference operation which should prove valuable in alerting one in such situations.) We may, as a result, be increasingly able to eliminate the interfering action of our own anxiety in dealing with that of the patient. On this rest the prospects of our patients' developing the capacity to expand their own awareness and hence reduce their anxiety-connected operations, and it is from this viewpoint that it seems worthwhile to report such observations as we have presented here.

BIBLIOGRAPHY

1. Fliess, Robert: The metapsychology of the analyst, Psychoanalyt. Quart. *11*:1942.
2. Winnicott, D. W.: Hate in the countertransference, Internat. J. Psycho.-Analysis *30*:1949.
3. Berman, Leo: Countertransference and attitudes of the analyst, Psychiatry *12*:1949.
4. Balint, Michael: Changing therapeutic aims and techniques in psychoanalysis. Internat. J. Psycho.-Analysis *31*: 1950.
5. Heimann, Paula: On counter-transference, Internat. J. Psycho.-Analysis *31*: 1950.
6. Reich, Annie: On countertransference, Internat. J. Psycho.-Analysis *32*: 1951.
7. Little, Margaret: Counter-transference and the patient's response to it, Internat. J. Psycho.-Analysis *32*: 1951.
8. Gitelson, Maxwell: The emotional position of the analyst in the psychoanalytic situation, Internat. J. Psycho.-Analysis *33*: 1952.
9. Cohen, Mabel B.: Countertransference and anxiety, Psychiatry *15*: 1952.
10. Fliess, Robert: Counter-transference and counter-identification, J. Am. Psychoanal. Assoc. *1*: 1953.
11. Weigert, Edith: Counter-transference and self-analysis of the psycho-analyst, Internat. J. Psycho.-Analysis *35*: 1954.
12. Glover, Edward: Countertransference and resistance, Chap. IV, Internat. J. Psycho.-Analysis. Supplement No. 3, 1928.
13. Coriat, Isador H.: Stammering: A psychoanalytic interpretation, Nerv. & Ment. Dis. Monograph Series No. 47, 1928.

ABSTRACTS

psychiatry

ADMINISTRATIVE PSYCHIATRY AND LEGAL ASPECTS OF PSYCHIATRY

81. *Medical Expert Testimony and Its Improvement.* WINFRED OVERHOLSER, Washington, D. C. J. M. Soc. New Jersey. *51*:133–141, April 1954.

The author discusses the evolution of medical expert testimony and the reasons for which it is often criticized. Among these are bias and apparent partisanship of the witness, the failure of courts to insist on adequate qualifications of the "expert," and the use of the hypothetical question. He recommends the adoption of procedures like the Briggs Law of Massachusetts and the Uniform Expert Testimony Act, proposed in 1938 but not yet enacted in toto in any state. He advises, too, more active "policing" by professional societies of the testimony of "experts," and a closer rapport between schools of law and of medicine. —*Author's abstract.*

For Reference

82. *Psychiatry and the Law.* WINFRED OVERHOLSER, Washington, D. C. Ment. Hyg. *38*: 243–251, April 1954.

83. *A Study of Administration of State Psychiatric Services.* RAYMOND G. FULLER. Ment. Hyg. *38*:177–235, April 1954.

BIOCHEMICAL, ENDOCRINOLOGIC, AND METABOLIC ASPECTS

84. *The Significance of Amino-Acids in Neuro-Psychiatric Diseases.* F. REITMAN, W. HULME, B. THOMAS, Coulsdon, Surrey, England. J. Ment. Sc. *100*:149–153, January 1954.

The presence of amino acids in the cerebrospinal fluid has been investigated in 30 unselected neuropsychiatric cases. The amino acid detection was by two-dimensional paper chromatography after the fluid was deproteinized and desalted. It was found that one group of cases had amino acids up to, and including, six in number, the other showing the presence of acids over that number.

The findings have been correlated to electroencephalographic (EEG) abnormalities and to clinical diagnostic groups. The EEG recordings have been evaluated for the purpose of this study as normal, abnormal, and severely abnormal. A statistically significant relationship was found between the presence of amino acids in excess of six and the occurrence of abnormal and severely abnormal EEG's. Both excess amino acids and abnormal EEG's

correlated with neuropsychiatric conditions that showed a well defined pathology and exhibited both psychiatric and neurologic symptoms. The correlation was statistically significant. The main psychiatric symptom to which the abnormalities correlated was cognitive deterioration. 5 references. 4 tables.—*Author's abstract.*

85. *Effect of L (+) Glutamic Acid on Mental Growth.* DOROTHY S. JAEGER-LEE, EMMA GILBERT, JOHN A. WASHINGTON, JONATHAN M. WILLIAMS, Washington, D. C. Dis. Nerv. System. *14*:368–385, December 1953.

The long-range effect of glutamic acid in mental and physical growth was studied in 101 mentally retarded children. The children ranged in age from a few weeks to 14 years, with I.Q.'s ranging from 30 to 100. For the purpose of analysis they were divided into two groups: those testable with the 1937 Revision of the Stanford-Binet (mental age of 2 years or more), and those not testable by this method (these were tested with Gesell Development Schedule). Cattell, Rorschach, and Goodenough tests were also used.

The data reported refer only to the group testable by Stanford-Binet, which was 51 per cent of the entire group. Each child received a thorough physical and neurologic examination. Complete blood counts, serum cholesterol, cephalin flocculation, and thymol turbidity tests, urinalysis, and x-ray of carpal bones were included in the study.

The dosage of glutamic acid varied according to the child's tolerance and willingness to take it in each case. The mother was instructed to increase the glutamic acid until the child developed symptoms of toxicity, such as irritability, sleeplessness, nausea and vomiting; then the dose was decreased slightly to the subtoxic level.

Placebos were also given the children (unknown to the parents). The cases were followed by several retests every six months on alternating forms L and M of the Binet, with repeat physical and blood studies.

Data on mental growth for 15 of these children were obtained for periods ranging up to eight years, and a mental growth curve was plotted. The mental growth of these same children was then plotted during treatment with glutamic acid, and a significant change in rate of mental growth was found.

For the entire group of 51 patients, the mean increase in I.Q. over the first six months of treatment with glutamic acid was 7.37 points; over 12 months 9.02 points; over 18 months 11.32 points; over 24 months 13.77 points. These results are all significant, with a probability of less than 1 part in 1,000.

When glutamic acid was discontinued with a change to placebo or no therapy there was a mean drop in I.Q. from the previous test of up to 6.68 points.

A discussion of comparison of results in this investigation with results in other investigations is included. 21 references. 5 figures. 4 tables.—*Author's abstract.*

86. *A Review: Psychological Responses to ACTH, Cortisone and Related Steroid Substances.* FRANK R. DRAKE, Denver, Colorado. Am. J. M. Sc. *227*:226–229, February 1954.

Since the original preliminary report of the sense of well-being associated with the use of Compound E and ACTH, a host of investigators has made further observations and studies of the psychologic responses to ACTH, cortisone, and related steroid substances. This

bright picture was soon somewhat clouded by reports such as that of Soffer and associates, which stated that 17 per cent of a group of patients with acute disseminated lupus erythematosus experienced severe depression and apathy. Other reactions, in confusing array, were classified as "schizoid reaction with catatonic features," "mild maniacal state," "paranoid disorientation," "hypomanic reaction," "near maniacal states," etc. Rome and Braceland brought some order into the classification of psychologic responses to ACTH and cortisone by dividing the range of responses into four descriptive grades. Grade 1 encompasses mild euphoric reactions. Grade 2 is merely a more marked response than grade 1, approaching the hypomanic level. About 60 per cent of their patients showed responses in grades 1 and 2. Grade 3 comprises every other variety of response short of overt psychosis and was found in 25 to 30 per cent of their patients. Grade 4 responses meet the criteria of psychotic reaction types and occurred in 10 per cent of their patients.

There is not complete agreement among investigators whether or not such factors as premorbid personality, type of somatic disease, or dosage of drugs used determine the psychologic response. In addition, there is no commonly accepted explanation of the mechanism underlying the secretion of anterior pituitary hormones. Recently there has been a renascence of interest in Cushing's syndrome because of the similarity between it and states of hyperadrenalism induced by ACTH and cortisone. Mental symptoms (including psychotic reactions) occur at times with both conditions. A number of years ago Allen and Broster described relief from schizophrenia in several cases following the removal of one overactive adrenal. In conclusion, it is obvious that the final determination of the true relationship of the pituitary-adrenal system to psychologic responses must await the combined efforts of many branches of medicine and surgery as well as the basic sciences. This is logical and to be expected, as feelings and emotions represent total body reactions rather than isolated phenomena, such as smiling with the lips (when happy) or clenching the fists (when angry). 15 references.—*Author's abstract.*

87. *Schizophrenia: A New Approach. II. Result of a Year's Research.* ABRAM HOFFER, HUMPHRY OSMOND, JOHN SMYTHIES, Saskatchewan, Canada. J. Ment. Sc. *100*:29–45, January 1954.

Following suggestions made in a previous paper ("Schizophrenia: A New Approach, I.") the authors have tried to substantiate their hypothesis that compounds exist in the chemical spectrum between Adrenalin and mescaline, which, while having psychologic effects like the latter, resemble the former in potency.

A series of clinical observations, combined with a careful study of known hallucinogens, directed their attention to the immediate breakdown products of Adrenalin itself, and in particular to those that occur in Adrenalin solution on standing. An enquiry of Professor Duncan Hutcheon of the Department of Pharmacology in the University of Saskatchewan suggested that this "pink Adrenalin" contained, among other things, adrenochrome. Further study of adrenochrome showed that its structural formula resembles that of all the known hallucinogens. Mr. Norman Eade and Professor Hutcheon undertook to make and test the toxicity of adrenochrome.

Once adrenochrome was synthesized, Hutcheon and Eade determined its toxicity and reported that it lowers the body temperature while increasing the metabolism, which suggests

that it has some direct central effect on the temperature-regulating mechanism. Professor V. Woodford, Jr. has found that adrenochrome markedly inhibits the intermediary metabolism of the cerebral cells. Drs. Szatmari and Hoffer have shown that, in people with epilepsy adrenochrome brought out cerebral dysrhythmias on the EEG more effectively than metrazol. This suggests that adrenochrome crosses the blood-brain barrier. An EEG tracing of this is shown in the text.

Once the toxicity of adrenochrome had been determined in animals by Hutcheon and Eade it was necessary to discover whether it had any psychologic effects on normal subjects. One tenth of a milligram was injected subcutaneously into a 200 pound volunteer, with no physiologic or psychologic effects apart from sharp pain at the site of injection. In the second experiment 0.5 mg. was injected subcutaneously into a 175 pound subject, with, after about 20 minutes, changes in thinking, affect, perception, and behavior which lasted for at least 12 hours. It is possible that more than 0.5 mg. was given in this second experiment. Further experiments suggest that 10 mg. is the minimal effective dose in humans and that it may cause psychologic disturbances for as long as 24 hours. The exact dose remains uncertain because of the instability of adrenochrome.

This is the first time that a substance that probably occurs in the human body, though this is not yet proved, has been shown to have psychologic properties of this sort. If there were an overproduction or a slowing in the detoxification of adrenochrome or something like it a condition resembling schizophrenia would result. As with other hallucinogens, adrenochrome should not be given to those who have suffered liver damage in the past. 20 references. 2 figures.—*Author's abstract.*

88. *Three-Year Follow-Up of Patients Developing Eosinophilia During Insulin Coma Therapy.* R. V. FREEMAN, T. E. JONES, J. J. PALMER, Los Angeles, Calif. Arch. Neurol. & Psychiat. *71*:501–510, April 1954.

When the rapid direct method of counting eosinophilic leukocytes became available in 1949, the attention of many investigators was directed toward the relationship between changes in eosinophile levels and the response of the pituitary-adrenal system to various types of somatic stress. We have done a three year follow-up survey of 11 patients, whose blood eosinophile levels were recorded in a consecutive series between January and September, 1950, as part of a pilot study of various metabolic changes during insulin coma therapy. These patients were young, male veterans of World War II, hospitalized because of an active paranoid psychosis. Treatments were given five days a week, until an average total of 32 comas was reached. On treatment days, insulin was administered intramuscularly at 7:00 A.M. and patients usually entered coma at about 9:00 A.M. Whenever possible, a short period of deep midbrain coma was attained at about 9:30 A.M., at which time direct eosinophile counts were done. Coma was terminated by dextrose by 10:00 A.M. The clinical response was evaluated during therapy and again three years later. The factors of behavioral improvement, symptomatic improvement, and the levels of social and occupational development were integrated, and the "response" defined as "improved" or "unimproved."

Statistical analysis of the 373 eosinophile counts done on these 11 patients during deepest coma revealed that definite eosinophilia developed in 7 patients, with the highest level

during the sixth weekly period, when the eosinophiles varied from 772 to 1,714 per cubic millimeter. During therapy, 6 of these 7 patients showed perceptible clinical improvement, but only 4 showed continued benefit of therapy after 3 years. A smaller group of 4 patients failed to manifest eosinophilia, and the level of eosinophiles at the sixth weekly period of treatment varied from 211 to 480 per cubic millimeter. Only one of this smaller group of 4 patients showed perceptible clinical improvement, and none was improved 3 years later. There was no strict relationship between the degree of clinical improvement and various factors, such as the age of the patient, the number of times deep coma was attained, the amount of insulin required to produce coma, or the degree of eosinophilia. As to the value of the eosinophile response as an aid in predicting the probability of prolonged remission of schizophrenia, our pilot study of 11 patients can only suggest that the development of eosinophilia, or perhaps some other, more reliable measure of response to somatic stress, may prove to be useful. 10 references. 1 figure. 1 table.—*Author's abstract.*

89. *On Pathologic Metabolic Conditions in Cases of Compulsive Neuroses (Ueber pathologische Stoffwechselbefunde bei Zwangskrankheiten).* HOLMER V. DITFURTH, Wuerzburg, Germany. *Nervenarzt. 24:*204–08, May 1953.

As certain vegetative ways of reacting correspond with certain constitutional conditions, it can be assumed that abnormal vegetative reactions may be coordinated to certain forms of psychopathy and in particular of obsession neuroses. The obsessive phenomena seem to be caused by anomalies in the diencephalic functions.

The author discusses 8 patients with obsessive neurosis who were examined for blood sugar reactions to insulin and Adrenalin. All of them had abnormal reactions. The common cause of this reaction seems to be an abnormally labile counteradjustment, which weakens or even abolishes the physiologic effect of the biochemical catalysts and must be regarded as an anomaly in the diencephalic function.

To disprove the objection that this coordination of a psychic with a vegetative anomaly may be observed also in cases of endogenous depressions with predominantly anancastic symptomatology, further experiments were made, which showed that the reaction of the latter patients was normal.

However, further research is necessary to prove with absolute certainty the coordination of the psychic and somatic symptomatology. The above-described findings may be typical not only for obsessional neuroses but also for other forms of mental disorder.

Examinations are being conducted to determine a biologically founded division between cases of proved abnormal vegetative constitution and cases in which the anomaly is confined to the psychic sphere. 41 references. 3 figures.

CLINICAL PSYCHIATRY

90. *The Recognition and Treatment of Anxiety States.* D. EWEN CAMERON, Montreal, Canada. Postgrad. Med. *15:*134–138, February 1954.

Anxiety states are among the most prevalent conditions with which physicians everywhere have to deal. They are encountered by the physician in three principal areas:

(1) The anxiety neuroses, which include anxiety, tensional states, and general anxious-mindedness.

(2) Anxiety states with severe somatization, where the presenting complaint is often a disturbance associated with the stomach, heart, breathing, and the skin. This is an area where I think the psychiatrist most frequently meets his colleagues in other fields of medicine and has to deal jointly with them in the management of these cases. I will elaborate this in detail shortly.

(3) The third and last great category of anxiety states comprises those occasioned by deficits, and I have listed these in alliterative sequence simply to demonstrate that they are so numerous that one can easily pick out a series of alliterations:

Coronary	Disfigurement
Cancer	Disability
Castration	Deprivation
Convulsion	Death

In this third group are anxieties caused by worry about coronary conditions, about cancer, about castration (I use the word *castration* with reference to women also), worry about convulsions, about disfigurement. And a tremendous cause of anxiety is disability, including, for instance, that which causes deep anxiety in a 56 year old teacher who is aware of a growing memory deficit as aging takes place prematurely. And there is deprivation, which Bowlby describes extraordinarily well in "Maternal Deprivation in Childhood," and its enormously destructive effects on the growing personality.

Recognition of anxiety should be a matter continually present in the physician's mind. Careful history taking will nearly always differentiate anxiety symptoms from others. In taking a history, I feel that there are four or five cardinal areas in which one has to make especially careful inquiries. First is the patient's statement. It is important to choose your phrasing. Sometimes people will say frankly that they are anxious and worried. More often, one has to go around it somewhat and say, "Are you tense?"

The next important question is, to what extent do the patient's symptoms cause limitation? Some major limitations are: Deeply anxious people cannot go into crowds; deeply anxious people do not want to be alone, as a rule; deeply anxious people cannot stand tension —difficulties and struggles around them: they become very upset by rows and will try to do everything possible to avoid them; deeply anxious people cannot stand stress for long—they become fatigued easily. A third general question concerns the patient's sleep and appetite. The fourth general question—and the most important one—is to determine whether or not there is a relationship between the intensification of symptoms and any incident in the surroundings. Here one meets considerable difficulties because patients very often invert things: for instance, I have a patient just now who has a lot of intermittent pain in the side of her head; she says that the pain prevents her going out and prevents her meeting people. Actually, careful tape recordings of her statements, played back and studied with her so that she can hear them again and again, show that the situation is really inverted: the pains come on when she gets into crowds; they are a localized symptom of tension in the scalp musculature engendered by her anxiety.

The *treatment* of anxiety states should be organismal, the patterns of treatment varying

with the kind of anxiety. In other words, the treatment approach to the patient should be at all possible levels.

An anxiety neurosis probably will not be cured by drugs alone. And, just as certainly, an anxiety state with severe somatization will improve rather slowly if one makes use of only psychotherapy. The drugs that are particularly useful are the barbiturates; and, more recently, we have been doing a good deal of experimental work with some of the new autonomic depressants, among them being Thorazine.

Psychotherapeutic methods, however, are of primary importance; and such methods—adequate for many cases, though not all—may be learned and used by any physician, provided attention is paid to certain basic principles. The first principle is listening—and most doctors think of the physician as someone who always performs an active role. The doctor, in his own mind and in the patient's, is the person who does something to you, who gives you a pill, who performs an operation, delivers you of a baby, and the like. In the field of psychotherapy this is not so. Here the doctor is no longer an active person but a collaborator who sits and listens. It is sometimes difficult for doctors to do this, but if you can listen and let the patient unfold, this will do him more good than any early intervention on your part.

The second principle is that explanations should come slowly and only after the patient has brought out all the relevant facts. The third principle is that the physician should be supportive and encouraging, but not to the point where the patient tends to become increasingly dependent.

Other useful methods in dealing with the anxiety states consist in the replanning of the individual's work and play. We see—and often enough among our colleagues—people who drive and drive and never relax, people who seek, as it were, salvation through work: if they aren't working, they feel mildly guilty. In general we find that the large-muscle recreations and those recreations that the individual can carry on at his own speed are the best. Hence, one recommends swimming, walking, gardening, fishing, and hunting. In replanning work, you can readily see that there are a number of jobs particularly likely to get tense, anxious people into trouble. For instance, there are deadline operations, such as those calling for the bringing out of advertising copy against a time limit, or writing a column for newspapers. Other jobs contain a very large degree of uncertainty and insecurity, such as stockbroking. Still others call for an unduly large amount of close attention to a limited number of activities. By and large, tense, anxious people do best when they can work at their own tempo and where there are a number of different activities to be entered into during the course of the day, such as in farming or as a traveling salesman.

Physiotherapy also has its place, in the form of massage and general diathermy.

There are certain guides in *selecting* people for psychotherapy. Among them are the following: Are they predisposed individuals? Have they been insecure since childhood? If so, they are going to be difficult to treat, because their patterns have become quite fixed. Are they people of poor motivation? Are they people who have a great deal to gain by the continuance of their illness? These more difficult cases should be referred to the psychiatrist. But the vast majority of anxiety states can be treated by physicians, no matter what their special fields may be.—*Author's abstract.*

91. *Major Neuropsychiatric Residuals Following Resuscitation from Cardiac Arrest; Preliminary Observations with Report of Three Cases.* RICHARD V. FREEMAN, LOUIS M. BERGER, SIDNEY COHN, WILBUR A. SELLE, Los Angeles, Calif. J.A.M.A. *155*:107–109, May 8, 1954.

The literature reveals 162 reported cases of heart massage following cardiac arrest, of which 35 per cent recovered completely or with minor residuals, while only 2 reported cases showed long-term major residuals. We add 3 cases in this hospital showing the latter outcome.

CASE 1. A 27 year old white male, injured in a fight, appeared apneic and pulseless in a hospital after a period estimated at from 5 to 15 minutes. Immediately on admission, manual cardiac massage was performed through a thoracotomy, and intravenous epinephrine was administered until spontaneous cardiac contractions resumed. For two weeks he was in profound coma, followed by gradual return of consciousness with marked ataxias, hyperactivity, and combativeness. Reambulation required long-term training, and ability to learn was grossly impaired. Two years later he shows no recall of any recent events, but he can recite the Gettysburg Address. He requires constant nursing care because of inattention and disorientation. Testing revealed an initial I. Q. of 52, now up to 73, and a general picture of constriction and withdrawal.

CASE 2. A white female, aged 29, sustained cardiac arrest incident to cyclopropane-oxygen endotracheal anesthesia during a dorsal sympathectomy for Raynaud's disease of four years' duration. Spontaneous contractions resumed after two manual compressions through a thoracotomy, total duration almost one minute. Deep coma for one day was followed by slow return of functioning. Electroencephalograms have been negative. Eighteen months later she requires hospital care because of ataxias, severe emotional lability, impaired orientation, and unusually short memory for recent events.

CASE 3. A white female, aged 27, sustained multiple fractures and head injury when struck by an auto. Although in deep coma, she received surgery for diaphragmatic hernia. Respiratory embarrassment necessitated tracheotomy, during which there was cardiac arrest. Manual massage was accomplished through a thoracotomy with return of spontaneous beat after 75 seconds' standstill. Recovery from coma was prolonged, with little return of function. Early electroencephalograms showed primarily base line sway with later return of 7–9 per second activity. Two years later she requires maximum nursing care because of a left spastic hemiplegia, right spastic hemiparesis, incontinence, noisiness, and inability to communicate. 13 references.—*Author's abstract.*

92. *Psychiatric Observations in Neurocirculatory Asthenia.* DANIEL W. BADAL, Cleveland, Ohio. J.A.M.A. *154*:1054–1058, March 27, 1954.

Neurocirculatory asthenia or effort syndrome has been the subject of a great deal of discussion and difference of opinion about its cause and position among diseases. This syndrome has a close resemblance to classic anxiety neurosis and is characterized by shortness of breath, palpitations, precordial pain or discomfort, easy fatigability and faintness, plus feelings of apprehension, nervousness, etc. Among psychiatrists and psychoanalysts it is generally regarded as a somatic equivalent of anxiety.

In the present study a group of enlisted men was examined in a controlled interview, with the following results: Phobic symptoms occurred in a high percentage of the patients, as contrasted to the normal subjects. In addition there is a strong hypochondriacal trend with a good deal of fixation on bodily symptomatology. In these soldiers, where exercise is very necessary as part of the job, it seemed that exercise itself had become the phobic object, and upon exposure to it the patient's anxiety increased greatly and the exercise intolerance increased. Individual case studies are given, illustrating the manner in which this phobic element had grown from a childhood neurosis in which personal conflicts were displaced to the body. It is as if the exercise intolerance and the anxiety about the body provide a point of displacement for subsequent anxieties. The childhood neurosis, which forms this basis, includes a sense of powerlessness and a need to be passive. When any situation occurs that calls up this feeling of powerlessness, anxiety occurs, which is then displaced to the body.

In conclusion, the effort syndrome can be considered not as a separate disorder but as a form of anxiety hysteria where the physical effort has become the phobic object.—*Author's abstract.*

93. *The Initial Interview.* WILLARD J. HENDRICKSON, ROBERT H. COFFER, JR., THOMAS N. CROSS, Ann Arbor, Mich. Arch. Neurol. & Psychiat. *71*:24–30, January 1954.

Traditionally, the initial psychiatric interview has been an occasion for a formal evaluation of the patient's "mental status"—his thinking, his emotional state, whether or not any hallucinations can be discovered, etc. In recent decades, due to the increasing understanding of the interpersonal relationships in psychotherapy, the emphasis has been less on a cold, formal evaluation and more on quietly listening to the patient recount his story and indirectly assessing his total picture and mental state. This seems to produce better results than a formal sort of "grilling" procedure. However, the initial interview should certainly be primarily diagnostic and evaluative, and only secondarily therapeutic. Various complications and problems that often arise in the initial interview are taken up, and we discussed the various areas that should be covered, and considered the value of brief, standardized tests for various psychologic functions. These seem useful at first glance but usually this is not borne out in later evaluations. They tend to introduce an atmosphere of interrogation which is quite at odds with the relationship the doctor has been striving to establish. 8 references.—*Author's abstract.*

94. *The Concept of Emotional Allergy (La notion d'allergie émotionelle).* P. SIVADON. Ann. méd.-psychol. *1*:239–43, February 1953.

An analysis of the symptomatology of cases designated as emotional allergy shows: (1) An allergic base, either a "neuroarthritic temperament" or an allergic phase following infection. (2) An experience regarded by the patient as involving danger and causing an emotional reaction, which is then minimized or blacked out. (3) The latent phase of several months to several years, during which there are symptoms of hypersomnia and daytime somnolence, and severe headaches, usually occipital or superorbital, more rarely bitemporal. (4) Some minimal emotional experience resembling or symbolic of the first emotional

experience. (5) After a short period of a few hours or a few days, the sudden development of symptoms of anxiety, agitation, confusion, delirium, or even of epilepsy. Six illustrative cases are reported and 1 is quoted from the literature. All these cases show the close relationship between the somatic allergy and the emotional shock. This may indicate that the psychosomatic problem does not involve an interaction between the mind and the body, but that there is an extension of a mechanism of reaction from one functional system to the other.

95. *On the Problem of Schizophrenia from the Point of View of Welfare Medicine (Zur Frage der versorgungsärztlichen Beurteilung der Schizophrenie).* ARNULF TIETZEN, Freiburg i/Br. Monatschr. f. Unfallh. *56*:104–07, April 1953.

After the First World War, the problem of the importance of exogenic factors of the pathography of schizophrenia was variously discussed, and since the last World War the discussion has been revived. Although, after the First World War, the etiologic relationships to abnormal psychic pressures were of prime interest, the interest has now turned toward the physical-organic influences of the outside and the damages done by them. The etiology of schizophrenia is unknown; however, heredity seems to be a main factor. Interestingly enough, the exogenous response to influences cannot be denied offhand. Psychic influences cannot be held responsible for schizophrenia; but traumatic, toxic, or infectious damages may very well be significant partial causes.

The evaluation of the consequences of dystrophy has played an important role in the judgment of the welfare physicians. In recent years, more and more neurologic-psychiatric pathographies have been described as consequences of dystrophy. It is generally assumed that under the special conditions of war captivity no remarkable increase in psychoses could be found, and the evaluation of a possible connection between schizophrenia and survived dystrophy is extremely difficult. Prolonged captivity may represent, however, an essential partial cause of an exogenetic character. It seems justified to deduce a connection, insofar as the hereditary weakness could be so aggravated that schizophrenia might be considered as the consequence of damages suffered. This was accepted in special cases of cranial and cerebral injuries and encephalitides, but a clear scientific foundation of this theory is impossible. If schizophrenia is considered a "somatosis" such a connection cannot be denied. The sure proof of organic damage to the brain and the existence of a direct temporary connection of the first symptoms of schizophrenia and the damaging event must be demanded. 38 references.

96. *Delusion of Parasitosis; Report of Successful Care with Antipellagrous Treatment.* IRMA ALESHIRE, Iowa City, Iowa. J.A.M.A. *155*:15–17, May 1, 1954.

A 62 year old woman had dementia with delusions of persecution and was refusing to eat. A psychiatrist thought this to be a senile psychosis. Several weeks later, after exposure to much sun, she was seen by the author. At that time she had pellagrous dermatitis and stomatitis, neurotic excoriations, and trichotillomania. There was a history of a grossly inadequate diet for some time. All the manifestations of her trouble disappeared with the use of an antipellagrous diet.

Because of the disappearance of this woman's neurotic excoriations it was decided to try antipellagrous care on similarly afflicted patients. Since that time, only 3 such patients have been seen. They all had delusions of parasitization by insects, accompanied in one 19 year old man by syphilophobia and a marked loss in memory and learning ability. This man had lesions resembling the nodular and vesicular forms of dermatitis herpetiformis, whereas the other 2 patients had only the usual crusted, dug-out areas and excoriations, with a superimposed dermatitis medicamentosa.

There were no gross signs of pellagra in any and no obvious signs of mental dysfunction other than their anxiety about their delusions of parasitosis. All gave a history of having felt the pricky bite of an insect, followed by a burning pain. In all 3 there was a history of a markedly poor diet. Their delusions, paresthesias, and skin manifestations were all cured by antipellagrous treatment. In addition, the man regained his memory, with increase in his learning ability. 3 references.—*Author's abstract.*

97. *Effect of Amobarbital (AMYTAL) and Affect on Conceptual Thinking in Schizophrenia, Depression, and Neurosis.* BERTRAM D. COHEN, RITA SENF, PAUL E. HUSTON, Iowa City, Iowa. Arch. Neurol. & Psychiat. *71*:171–180, February 1954.

Conceptual thinking was studied with a new object-sorting technic in chronic schizophrenic, depressive, and neurotic patients under four test conditions: neutral; affective (using affect-arousing objects); drug (intravenous amobarbital sodium and amphetamine sulfate); and affective-drug. The results indicated impaired conceptual thinking in schizophrenia, which, however, was not diagnostic. In response to experimental manipulation, affective objects impaired thinking in the depressive group but not in the others. Drugs alone impaired the depressive group, improved the neurotic, and did not affect the schizophrenic groups. All groups performed most poorly on the affective-drug test. Theoretical implications of these findings are discussed. 16 references. 1 figure. 2 tables.—*Author's abstract.*

HEREDITY, EUGENICS, AND CONSTITUTION

98. *The Cerebral Ventricles in Dementia Praecox (Les ventricules cérébraux dans la démence précoce).* F. MOREL, E. WILDI, Geneva, Switzerland. Monatschr. f. Psychiat. u. Neurol. *127*:1–10, January 1954.

A ventriculometric study was made of the brains of 59 schizophrenic patients; it showed that the lateral ventricles were smaller than the average as measured in several hundred brains from psychiatric patients. When comparison was made with the curve of ventricular capacity in relation to age, the deviation in the schizophrenics was found to be statistically significant. The small capacity of the ventricles in schizophrenia is a constitutional anomaly; in a considerable number of the brains examined, intraventricular adhesions were present. 8 references. 3 figures.

PSYCHIATRY AND GENERAL MEDICINE

99. *The Treatment of Psychosomatic Disorders by the Internist.* HERBERT I. HARRIS, CAREY M. PETERS, Cambridge, Mass. Am. Pract. *5*:158–163, March 1954.

The 40 to 70 per cent of patients suffering from psychosomatic disorders have not in the past been effectively treated by internists or general practitioners. The availability of modern methods of psychotherapy now makes this possible; they are outlined in this paper. Cases of varying degrees of severity are described and the method of treatment in each case discussed. Emphasis is placed repeatedly upon the importance of the internist-psychiatrist relationship, in which the internist serves an apprenticeship to a psychiatrist trained in the newer modalities of psychotherapy. This professional relationship parallels that of the internist developing skill in cardiology, hematology, electrocardiography, or other subspecialty. The authors feel that in extending his competence over the field of psychosomatic disorders the internist is recapturing the art of medicine and enriching his own practice and life with the insights which he acquires by engaging in this form of treatment. Before embarking on such psychotherapy, thorough medical history, physical examination, and laboratory study will, of course, be done. 12 references.—*Author's abstract.*

100. *Somatopsychic Medicine.* JOSEPH WILDER, New York, N. Y. Am. J. Psychotherapy. *8*:43–53, January 1954.

The author emphasizes that we live not only in a psychiatric era in medicine but also in the medical era in psychiatry. Since both somatic and psychologic psychiatry are in the middle of a marked development a better integration should be possible. One recent neomechanistic attempt of that kind is cybernetics. The progress in genetics is not spectacular. New technics are applied in brain physiology, such as registration of remote electroencephalographic changes on brain stimulation; the detection of the activator system in the brain stem by Magoun and co-workers is the most fruitful result. The various forms of brain operations afford an unprecedented field of experimentation, especially when performed on normal persons for intractable pain. Fulton's concept of the visceral part of the frontal lobes could thus be confirmed. Self-experiments and experiments on patients with such drugs as mescaline, benzedrine, actedon, d-lysergic acid are being continued. In the biochemistry of the brain the interest has turned toward the carbohydrate and recently toward the protein metabolism of the brain (nucleic acid, glutamic acid). The patients saved after prolonged heart arrest afford a special opportunity for the study of the effect of anoxia on the physiology and pathology of the brain. The study of effects of poisons of the brain continues with constantly new medicinal and industrial poisons added. The author mentions his own contributions in the studies of changes in the blood cholesterol curve in psychotic depressions and the relation of uric acid to psychoses. In the study of the effect of hormones on the brain and psyche, cortisone and ACTH, with their marked psychic effects, have opened new vistas. Such clinical entities as phenylpyruvic oligophrenia, gargoylism, mental deficiencies in kernicterus have been added in recent years. Unfortunately the clinical picture of psychosis or neurosis in organic disease has not yet been firmly established, with the result that many patients with temporarily negative somatic

findings are forced to go on in life often developing a superstructure of an iatrogenic neurosis, which disappears promptly once the somatic diagnosis is made. Examples of psychosis in pernicious anemia, cyst of the septum pellucidum, Cushing's disease, latent postencephalitic parkinsonism, and oral sepsis are quoted. 26 references.—*Author's abstract.*

101. *Psychologic Implications of Cancer.* JOOST A. M. MEERLOO, New York, N. Y. Geriatrics. *9*:154–156, April 1954.

A survey of the emotional problems of cancer helps only when one can transpose these observations to daily clinical experience. A tendency to get away from psychologic implications may be present in both patient and therapist. Cancer is always associated with death, and thinking of, as well as having feelings about, death is taboo. The fears aroused by malignancy—fear of mutilation, of drastic change, and of death—make it essential that the physician be aware of psychologic aspects in the patient, in the patient's family, and in himself as well.

Beyond this, the author raises twelve different points of eventual or additional emotional etiology, which can be explored as an honest scientific proposal, founded on varied clinical experience. A solution will be reached only through intensive teamwork among biochemist, surgeon, psychologist, and anthropologist.—*Author's abstract.*

For Reference

102. *The Importance of Depressive Reactions in Clinical Medicine.* WILLIAM KARLINER, New York, N. Y. Am. Pract. *5*:361–363, May 1954.
11 references.

PSYCHOLOGIC METHODS

103. *Results of the Rorschach Test Given to Obsessional Neurotics (Rorschachbefunde bei Zwangsneurotiken).* CHRISTIAN MÜLLER, Burghölzli-Zurich, Switzerland. Schweiz. Arch. f. Neurol. u. Psychiat. *72*:226–31, 1953.

The author feels that the Rorschach test does not apply itself to obsessional neuroses so well as heretofore assumed. The obsessional neurosis is not absolutely determined by this test as of the "grasping" (*Erfassungs*) or the "experiencing" (*Erlebnis*) type, nor is there a uniform appearance of the HD—Dzw—Dd—and Do answers.

No differentiation can be derived between obsessive patients who are inclined to obsessive action and those who have obsessive ideas.

The Rorschach experiment is, in the author's opinion, a valuable momentary picture of the personality, but it is always influenced by other factors that prevent a deeper analysis such as the careful, clinical exploration provides. 8 references.

104. *The Varying Response to Pain in Psychiatric Disorders: A Study in Abnormal Psychology.* K. R. L. HALL, E. STRIDE, Bristol, England. Brit. J. M. Psychol. *27*:49–60, March 1954.

The primary concern of this study has been to focus attention on response to pain as an indicator of personality characteristics or attitudes that may be quite general or consistent

within the individual although possibly accentuated in the abnormal mental conditions investigated. All the chief factors that have been suggested to account for variation in response to pain—age, sex, intelligence level, neurotic disturbance—can be classed as attitude factors and investigated as such. The evaluation of these general factors has been attempted within the psychiatric population studied, both by direct observation under a standard condition and by experimental variations of conditions.

Some 400 patients with diagnoses of neurosis or depression, together with a small group of schizophrenics, were studied using a modified version of the Hardy-Wolff apparatus. The patients were of both sexes and covered an age range of between 18 and 70 years. Under the standard procedure (condition 1) the instructions were such as to induce an expectancy of a painful experience. Two minor experiments, in which the instructions were modified, were carried out: in condition 2 no instructional set was given that the patient was about to experience a painful stimulus, and in condition 3 an attempt was made to induce an objective attitude in the patients. Under each condition three measures of response to pain were recorded, viz: warmth perception point, verbal report of pain, and pain reaction point.

The results of the investigation showed that age and sex were two highly significant factors accounting for a large part of the variability shown under the standard procedure. The older the patient, the greater the probability of a high verbal report of pain and a high pain reaction point, and female patients of comparable age and clinical category were found to report pain earlier than males. The warmth perception point was relatively unaffected by either of these two factors, and neither age nor sex was found to influence any of the three measures recorded under conditions 2 and 3.

Patients of the depressive and schizophrenic categories tended to report pain at a uniformly high level, irrespective of age, and this high pain tolerance appeared to be arrived at in at least two ways. In schizophrenic patients and certain types of depressives the high verbal report of pain appeared to be but one aspect of a general unresponsiveness to external stimuli. In other depressions and certain of the mixed-neurotic conditions the high pain tolerance appeared to be due to an inhibitory attitude more or less confined in its effect to unpleasant stimuli, fatigue feelings, etc., the response to neutral stimuli being within the normal range. A further finding on depressive patients was that those who showed clinical improvement after E.C.T. also showed a highly significant lowering of pain response in comparison with retest results of a group of similar patients who were untreated or unimproved.

The early responsiveness of anxiety neurotics was shown to be largely the result of an anticipation of a painful experience induced by the mental set of the instructions, although this tendency was reduced with increasing age.

These results are interpreted as demonstrating some of the central attitude factors responsible for the wide variability in the response to pain within these particular groups of psychiatric patients. Although constitutional and innate temperamental differences may obviously contribute to this variability, an explanation is attempted primarily in terms of conditioning and learning of habitual response patterns—for example, conditioned avoidance response in anxious patients, and conditioned inhibition in some depressed patients. This seems to offer a sound basis both for analysis of the present experimental observations

and for the further investigation of the many problems in abnormal response to pain that have arisen in the course of this study. 31 references. 4 figures. 1 table.—*Author's abstract*

PSYCHOPATHOLOGY

105. *A Re-examination of Some Aspects of Conversion Hysteria.* PAUL CHODOFF, Washington, D. C. Psychiatry. *17*:75–81, February 1954.

The author considers some of the reasons why hysteria is diagnosed less often than previously; the relationship between anxiety and conversion as exemplified in the phenomenon of "la belle indifférence;" and the role of repressed hostile impulses in the psychogenesis of conversion phenomena.

The less frequent diagnosis of hysteria may be ascribed partly to the increased separation of neurology and psychiatry; many psychiatrists are incompetent in neurology and do not discover areas of analgesia and anesthesia. In any event they are more interested in psychoneurotic manifestations as whole or part reactions of total personalities than in specific diagnoses. In addition, with the rise of psychosomatic medicine, many psychosomatic symptoms of emotional origin are no longer considered to be conversion manifestations. Yet conversion phenomena undoubtedly do occur less frequently than formerly; this decrease can be attributed in part to a change in the cultural climate, as a result of which these manifestations have been largely replaced by anxiety reactions and by obsessive and phobic defenses against anxiety. People are not so simple and unsophisticated as they used to be, and are less prone to the development of the crude and gross manifestations of conversion hysteria. Again, the prudery and sexual inhibitions of the 19th century are less pervasive and influential now.

"La belle indifférence," or the hysteric's placid lack of concern over his disability, has always been considered pathognomonic of hysteria, on the assumption that there is usually an inverse ratio between overt anxiety and conversion phenomena. That "la belle indifférence" is present in all or even the majority of patients with hysteria is not true, in the author's opinion. When this phenomenon actually occurs it represents a denial not only of the original repressed material but also of the conversion phenomena. Such a denial is more likely to occur in the classic hysterical personality, and less likely to occur when conversion phenomena appear in obsessive patients or schizophrenics.

In conversion hysteria, the emphasis has been put on unacceptable erotic drives as being the most important constituent of the repressed material. It is suggested here that dissociated hostile impulses, alone or in association with erotic or dependent components, may play an important role and that closer attention to these may be helpful in psychotherapy of hysterics. There is evidence of the importance of hostility in these patients in the commonly felt hostility toward hysterics; the effect produced by a psychoneurotic activity is often the one unconsciously intended. 23 references.—*Author's abstract.*

106. *Psychotherapy of Schizophrenia and Borderline Cases (Psychotherapie bei Schizophrenien und Uebergangsformen).* ELSA KOCKEL, Zurich, Switzerland. Schweiz. Arch. f. Neurol. u. Psychiat. *72*:187–210, 1953.

The author describes at length several cases she selected from patients whom she ob-

served during a 10 year period. All of them were mild cases, which could be treated in the office.

In order to determine the right treatment from the beginning and avoid any damage, a correct diagnosis of borderline cases, as well as mild or latent forms of schizophrenia, seems of importance; even small symptoms, which may appear only imponderable, should not be overlooked.

The prognosis for the borderline cases is not unfavorable, although there will remain certain difficulties in making contact and slight paranoid ideas. This leads to the conclusion that the etiology of the schizophrenia rests mainly on constitutional factors and more so than do neuroses. All the patients appeared to lack the courage to open themselves to the other person and the world because they had missed parental affection. The patients themselves were of great help in the psychotherapy as soon as this want of affection could be released. However, a deeper delving into the personal history often had a traumatic effect and caused an aggravation in the condition. It seems advisable, therefore, to go into the interpretation of personal experiences only slowly and after an improvement in the condition has been attained.

The author re-emphasizes the bearing on the illness of the always deep rooted conflict with one of the parents. This leads her into a discussion of mythology. It seems obvious to her that the rites described in old as well as modern writings have a definite and deep meaning—the Dionysiac mythology can be interpreted only as a most intimate contact with the symbols of the mother and immortality, i.e. a continuity of time and eternity.

In all the cases discussed in this article the personality had been unbalanced because this continuity, the continuity of ancestry and time, had been interrupted. The patients, therefore, had to be shown the symbols of continuity in order to be given security and freed from their fears.

107. *On Creative Functions in the Beginning of Schizophrenic Psychoses* (*Ueber schöpferische Leistungen im Beginn schizophrener Psychosen*). O. H. ARNOLD, Vienna, Austria. Wien. Ztschr. f. Nervenheilk. *7*:188–206, 1953.

From the examination of schizophrenic patients for the causal conditions of their creative functions, three criteria have become apparent:

1. Subjective: The experience of something new with a sensation of being overwhelmed, almost as if intoxicated.

2. Objective: The realization of the idealistic in spite and because of the resistance of the material.

3. Biologic: The elevation of a human or interhuman function in a quantitatively developing leap to a new and higher organizational level.

To determine to what extent the contents of these functions represent specific schizophrenic changes, 53 of thousands of patients were singled out and evaluated for general characteristics.

It was found that there really are general symptoms, the genesis of which was watched with a view to discovering a formal change in the process of experiencing. Formal variations from the normal experience occur physiologically under the influence of drugs and in specific nuances of schizophrenia.

It is demonstrated that a specific schizophrenic change in the process of experiencing pushes the patient into a defensive reaction, the visible results of which are the creative functions of the incipient schizophrenic psychoses. 26 references.

108. *The Transition of Obsession Neuroses into Schizophrenia in the Light of the Catamnesis (Der Uebergang von Zwangsneurosen in Schizophrenie im Lichte der Katamnese).* CHRISTIAN MÜLLER, Burghölzli-Zurich, Switzerland. Schweiz. Arch. f. Neurol. u. Psychiat. *72*:218–25, 1953.

The problem of the transition of obsessional neurosis into schizophrenia no longer seems to hold the same interest it held in former years. However, only a few publications on the subject of catamneses have appeared that cover a long period of time, and it remains open to question what psychologic understanding of the development of the illness out of early obsessive neurotic stages can be derived from the modern psychodynamic theories.

Only 40 years ago, the obsessional symptoms were definitely attributed to the manic-depressive or the schizophrenic cycle. But it is indispensable to compare obsessive occurrences with endogenous psychoses. The author enters into a discussion of various theories on obsessional neuroses and schizophrenia, which he follows up with a description of his own case material, limiting himself to four questions:

1. How often does the transition occur?
2. How do these psychoses develop?
3. Can differences be observed between those obsessive patients who became psychotic and those who did not?
4. Can prognostic conclusions for the course of the psychosis be drawn from the duration of the prepsychotic obsessional stage?

1. About 15 per cent (9 of 57) of the obsessional neurotics became psychotic. Among the psychoses of early obsessive neurotics, schizophrenia greatly outnumbered the manic-depressives (7:2).

2. The course the schizophrenia took in early obsessional neurotics seemed not to differ discernibly from that of all other schizophrenics.

3. In the author's case material, the schizophrenia of the early obsessional neurotics took a particularly grave course if the obsessional neurotic phase was of a short duration and schizophrenic symptoms set in early.

4. The prepsychotic obsessional phase of later schizophrenia that took a comparatively benign course did not appear to be different from a pure obsessional neurosis that remained permanent. The later schizophrenia that took an unfavorable course, however, differed from the real obsessional neuroses insofar as the patient developed a particularly strong fear complex during the obsessive phase. 21 references.

109. *On the "Anatomy" of Hypochondriac Conditions (Zur "Anatomie" hypochondrischer Zustände).* HANS E. KEHRER, Münster/Westphalen, Germany. Arch. f. Psychiat. & Nervenkrank. *190*:449–60, August 1953.

Based on the observation of 40 hospital patients, the author discusses certain pathogenetic connections between hypochondriac symptoms and atrophic processes in the brain.

Hypochondriac behavior is a symptom that accompanies various groups of diseases such as cyclothymia and schizophrenia, but it occurs also without other psychic symptoms. In nearly all the patients who showed hypochondriac tendencies, a rather uniform organic change in the brain could be observed, not at all characteristic of these above mentioned mental diseases, namely atrophic changes of various degrees.

Of the 40 patients who underwent the encephalographic examination, 39 suffered from such atrophy, especially in the parietal lobe. The prevalent causes seemed to be circulatory disturbances in the cerebral blood vessels, in some cases caused by arteriosclerosis, and possibly also focal infections. All patients described the same complaints, which lacked an organic foundation.

Hypochondriac conditions should not be taken lightly; most of these patients are seriously ill. The localization of the atrophy in the parietal cerebellum may indicate a disturbance in the center of the critical sensory zone. This finding should determine the treatment of the patients. 2 tables. 4 figures. 14 references.

For Reference

110. *The Application of Cybernetics to Psychiatry.* W. ROSS ASHBY, Gloucester, England. J. Ment. Sc. *100*:114–124, January 1954.
7 references. 1 figure.

111. *Depression, Hypomania and Depersonalization.* H. ROBERT BLANK, White Plains, N. Y. Psychoanal. Quart. *23*:20–37, January 1954.

A 23 year old girl suffered from depression, hypomania, and depersonalization, which were associated with many hysterical symptoms and frequently occurred in attacks, before and during the analysis, the meaning of which repeatedly could be ascertained. She was severely masochistic, for example: several weeks before treatment began she became pregnant, sleeping with one lover on Saturday, with the other on Sunday. She was terrified by a Rorschach test; two hours after the test she broke out in giant hives covering her entire face and body. She epitomized her relationship with men as follows: "The man is either a big blob of fat crushing me or he is a tiny mosquito trying to get into me."

Five attacks are described, the fifth sufficing here to demonstrate the pattern. Toward the end of the second year of analysis the patient became acutely depressed following a severe disappointment in love. She was struggling at the same time to control her feelings about the impending five week analytic vacation. During the session in which all this emerged she stated she knew what she wanted from the analyst was impossible because she was not a baby and he was not a parent. Following the session, the patient had to telephone an analyst-employer for whom she did part time work in order to learn whether he wanted her that afternoon. There was a half hour delay before she could reach him, so she stepped into a five-and-ten-cent store. Although she had felt depressed and angry with the analyst on leaving the session, in the store she suddenly felt a strange freedom, an urge to spend money on lipstick and a lot of trinkets that she did not need; she was "hopped-up" and elated. As she left the five-and-ten to make the call she was suddenly overcome by a feeling of unreality, the typical "dead" and "dreamlike" feeling. She called her lover, which

reassured her, then called the employer, who told her he had been trying to reach her and wanted her to come to work, and soon she was over the attack, which had lasted a half hour.

The patient's associations to the elements of the entire episode were obtained. To the five-and-ten where she had had the hypomanic attack, she promptly associated, "my great delight when I was 5 or 6 spending money at the five-and-ten. I would ask Mother for a dime, which she gave me." She would buy rings, which she put on her finger so she might pretend she was married just like her mother.

In this attack the following sequence is plain: intense feelings of frustration and deprivation; anger and depression; denial of the deprivation by the hypomania, with its elation and clear content of love from and identification with the good mother; restoration, by her leaving the store, of the disillusioning reality of her multiple responsibilities, the analyst's deserting her, the employer-analyst's being unreachable; blotting out of the threatened overwhelming painful reactions by acute depersonalization.

The writer regards the symptoms of depression, hypomania, and depersonalization in this patient as major elements in a hierarchy of defenses against anxiety arising from unresolved oral conflicts. The hypomanic episodes confirm Bertram Lewin's thesis that hypomania represents a denial of the deprivation basic to depression, elation signaling gratification by and fusion with the mother. Depersonalization seemed to be an emergency defense against the threatened eruption into consciousness of a massive complex of feelings of deprivation rage and anxiety. There was also an indication that depersonalization was called into play when the hypomanic defense (denial) failed to keep the dangerous affects in repression.

An attempt is made to correlate the symptoms selected for special study with the patient's other prominent symptoms and character traits, notably her severe sleep-walking disturbance and masochism, and with the phenomena of normal sleep. 6 references.—*Author's abstract.*

TREATMENT

a. general psychiatric therapy

112. *The Conditioned Reflex in the Chronic Schizophrenic.* H. N. PETERS, O. D. MURPHREE, North Little Rock, Ark. J. Clin. Psychol. *10*:126–130, April 1954.

In an extensive investigation of guided problem-solving under hunger motivation (cf. Peters & Jenkins, *Psychiat. Quart.*, 1954) as a method of treating chronic schizophrenics, it was found that after three months of treatment the patients were in improved clinical condition. Conclusions were based on comparisons of groups of treated and untreated patients. This paper reports the results of an investigation of conditioning the galvanic skin reflex in randomly selected groups of treated and untreated patients, and in two small groups of normal subjects.

Two separate experiments, with different experimenters and different subjects, were done. The unconditioned stimulus was a loud horn in one experiment, weak palmer electric shock in the other. Red and green lights were used as conditioned stimuli in both experiments.

Treatment of the data (ink polygraph recordings of galvanometer deflections) supports two conclusions: (1) The autonomic response to unconditioned stimuli is greater in the

normals and treated patients than it is in untreated patients. (2) Normals and treated patients are more readily conditioned, on the autonomic level, than are untreated patients. Results are interpreted as objective evidence of the effectiveness of guided problem-solving as therapy in chronic schizophrenics. 7 references. 3 tables.—*Author's abstract.*

113. *Treatment of Elderly Psychiatric Patients; Use of a Diagnostic Classification.* VERA NORRIS, FELIX POST, London, England. Brit. M. J. *1*:675–679, March 20, 1954.

It is now recognized that mental illness in old age does not connote incurable illness. Psychiatric treatment gives successful results if applied to the right type of patient. The authors wished to show the utility of a simple diagnostic assessment of the patient made at an outpatient consultation. A three point classification was used: (1) dementias of old age, i.e. irreversible disorganizations of personality due to degenerative brain changes; (2) long-standing neurotic, psychotic, or character disorders; (3) recent reactions, either affective or toxic-confusional. The following treatment recommendations were made: (a) active psychiatric treatment as a hospital in- or outpatient; (b) no special psychiatric therapy, but supervisional care at home or in hospitals for long term nursing care. Active psychiatric treatment included not only physical treatment but any type of planned psychiatric treatment (e.g. social, environmental, or psychotherapeutic).

The 192 patients in this series were all over 60 years of age, and one quarter over 70 years. The examination of both mental and physical health took between 45 and 75 minutes, and on this the diagnosis and treatment recommendation were made. The success of the initial diagnostic assessment was measured by the status of the patient after one year. Of patients diagnosed as recent affective psychotics 78 per cent received active treatment, whereas among long-standing cases and also among organic psychoses only 21 per cent of the patients were considered likely to benefit from active treatment. Of 109 affective psychotics there were 18 patients who showed atypical features. The outcome of treatment recommendations was successfully predicted in 90 per cent of the typical, but only 55 per cent of the atypical, cases. In the long-standing group 9 out of 33 were atypical, and in the organic group 13 out of 46 were atypical. In both these groups the outcome was successfully predicted in three-quarters of the typical and only one-half of the atypical cases. Thus it was easier to recommend the best course of action in typical cases. In this series the diagnosis was made after a single outpatient consultation. The simple diagnostic classification used acted as a useful screening method, which enabled the limited facilities available for active psychiatric treatment of the elderly to be used to the best advantage. Even among these patients affective illnesses of recent origin show an immediate favorable response to active treatment. 5 references. 6 tables.—*Author's abstract.*

b. drug therapies

114. *Chlorpromazine; New Inhibiting Agent for Psychomotor Excitement and Manic States.* H. E. LEHMANN, G. H. HANRAHAN, Montreal, Canada. Arch. Neurol. & Psychiat. *71*: 227–237, February 1954.

Chlorpromazine is a phenothiazine derivative that was developed in France, where the first pharmacologic and clinical investigations with the new drug were carried out. The sub-

stance seems to possess specific properties for the psychiatric management of excited states.

Chemically related to promethazine (Phenergan) and diethazine hydrochloride (Diparcol), Chlorpromazine has pronounced anti-emetic action, exhibits moderate antihistaminic activity, mild adrenergic blocking, and marked potentiating effect when it is administered in combination with cerebral depressants. The major proportion is metabolized in the organism before it reaches the kidneys.

In humans, Chlorpromazine produces a pronounced drop in blood pressure and a compensatory tachycardia. Hypothermia is usually observed in animals, but in humans occurs only occasionally. The respiratory rate is not influenced by the drug. The appetite remains good. Dryness of the mucus membranes occurs frequently.

Motor retardation, a wooden facial expression, and marked drowsiness during the first days of treatment are striking effects on the central nervous system.

Chlorpromazine was given to 71 psychiatric patients ranging in age from 18 to 82 years over a four month period. It was found to be of unique value in the symptomatic control of almost any kind of severe excitement, including catatonic schizophrenia, schizo-affective conditions, epileptic clouded states, agitation in lobotomized patients, and organic toxic confusional states.

The most favorable therapeutic results were obtained in manic-depressive patients in the manic state. The drug seemed to shorten the individual attack significantly, and fewer relapses occurred than with electroshock treatment. In a few cases, the authors had the impression that the immediate administration of the drug for three or four days prevented a psychotic breakdown in patients who were exhibiting typical prodromal symptoms.

Doses vary considerably with the individual. Tolerance develops within a few days, and parenteral administration produces more reliable effects than oral. In states of severe excitement, 50 mg. may be given intramuscularly twice a day, with 50 mg. added orally two or three times a day. Doses may be rapidly increased, but bed rest is mandatory at least during the first two days because of the high incidence of postural hypotension. Blood pressure, pulse, and temperature should be recorded at least twice a day. The authors have rarely exceeded a dose of 800 mg. a day. In acute psychotic excitement the aim is to produce a state of motor retardation, emotional indifference, and somnolence.

In less pronounced psychomotor restlessness or emotional tension, 25 to 50 mg. two to four times a day orally may be sufficient. The course of treatment may last from three days to four weeks or may even be extended over several months.

Side effects and complications include nausea, anorexia, and epigastric distress, allergic reactions (urticaria, asthma); and in 3 patients jaundice developed, which subsided within 10 days after the drug was discontinued. The authors stress that Chlorpromazine must be administered under close medical supervision, and larger doses over extended periods of time should preferably be given in a hospital setting. Caution is indicated in patients with impaired liver function.

Psychologic tests demonstrated that the higher psychic functions involving attention and learning are preserved to a remarkable degree in patients who are under the influence of Chlorpromazine. This drug differs in its action from most other known sedatives in that it does not seem to produce clouding of consciousness, impairment of judgment, or disinhibition of affect. It tends to produce an attitude of sober resignation and of critical reflection. In

contrast to barbiturates, it does not alter the basic character of the individual EEG as long as the subject is awake, which indicates that cortical metabolism is little affected by Chlorpromazine. Patients receiving the drug become lethargic, display a lack of spontaneous interest in the environment, yet are easily accessible and respond as a rule immediately and relevantly to questions if stimulated. The drug selectively inhibits drive. It is speculated that the site of its action is in the activating reticular substance and in the hypothalamus. The possible chemical mechanism of Chlorpromazine may involve antiacetylcholine properties in the neuraxis, which have been shown to exist in chemical substances closely related to it. 10 references. 1 table.—*Author's abstract.*

115. *The Effect of Drugs on Group Therapy: An Experiment.* C. H. CAHN, Montreal, Canada. J. Nerv. & Ment. Dis. *118*:516–526, December 1953.

Eight patients were selected who, it was thought, might benefit from group therapy. Sessions were held twice a week for eight weeks. Patients were given caffeine citrate, Benzedrine sulfate, Seconal, or Sodium Amytal one hour before each session. The drugs were given in the form of two white capsules so that the patients would not know what they were receiving. As a control they were given two capsules of glucose every third session.

To make the atmosphere congenial, peanuts and cigarettes were provided freely. The group leader assumed a permissive attitude, and he acted as a catalyst to the discussions whenever possible. An observer recorded how often and how long each patient spoke, the main subject matter under discussion, and the number of interruptions and digressions per session. After each session the number of peanuts consumed and cigarettes smoked were counted. The patients cooperated fully throughout the duration of the experiment.

All the sessions were fairly lively, but the liveliest by far occurred after the patients had been given 10 mg. of Benzedrine sulfate. All the barbiturate sessions were lively, on the average more so than the glucose control sessions; and even with 2¼ gr. (0.15 Gm.) of Seconal all the patients were alert, the discussion was free and productive, and no marked sedative (and not to mention hypnotic) effect was noticed. The caffeine sessions approximated the glucose control sessions and thus were not conclusive.

It was found that the total number of times the participants spoke and the number of interruptions per session provided a fairly good index of the mental level of activity, and the number of peanuts consumed per session could be translated into a scale of motor activity of the group. Usually, during a lively meeting, all these quantities were higher than during a quieter one, except when 10 mg. of Benzedrine sulfate had been given, when the peanut consumption was relatively low. The number of cigarettes smoked per session was too small to provide any statistically significant data.

The main conclusion drawn from the experiment was that both Benzedrine and the barbiturates increased social interaction and stimulated the discussions. On the whole, however, barbiturate was preferable to Benzedrine in that the former did not bring out, as much as the latter, aggressive tendencies of the patients that interfered with the smooth and uninterrupted flow of conversation. 4 references. 3 figures. 2 tables.—*Author's abstract.*

neurology

CLINICAL NEUROLOGY

116. *Clinical Observations on Aphasia.* HILDRED SCHUELL, Minneapolis, Minn. Neurology. *4*:179–189, March 1954.

Sixty-five aphasic patients were examined at the Minneapolis Veterans Administration Hospital by means of a diagnostic battery of tests developed in the aphasia division of the neurology service. No isolated pure disorders of any language function were observed, and partial rather than total disabilities were usually found. Although individual responses were variable, percentages of correct responses were stable, and consistent patterns of impairment emerged.

All patients showed impairment of auditory processes. Those who showed impairment of auditory recognition tended not to recover functional speech. Impairment of auditory retention appeared to be reversible.

Patients with visual involvement confused symbols with similar visual configurations, produced reversals and distortions of symbols, and had difficulty following the line and keeping the place in reading. They often had difficulty revisualizing both objects and symbols and showed signs of spatial disorientation. On higher levels reading disabilities stemmed from impairment of auditory retention.

Speech disabilities stemmed from involvement of motor processes and impairment of word finding, which, because of correlations observed, was considered to stem from impairment of auditory recall. Impairment of formulation appeared closely related to impairment of auditory retention and improved as retention improved.

Impairment of writing was traceable to motor impairment, visual impairment, or both, and on higher levels both auditory retention and recall were involved.

Three recurring patterns of impairment were identified: (1) a pattern of severe damage; (2) a syndrome based on impairment of auditory retention and recall, and (3) this same pattern complicated by co-existing motor involvement, visual involvement, or generalized brain damage with mental deterioration.

No patients in the first group recovered functional speech. Prognosis for the second group is excellent. Patients with co-existing motor disabilities commonly acquired usable speech, but more slowly, and speech tended to remain limited and defective for a long time. Patients with visual involvement superimposed on the basic syndrome followed normal recovery curves for speech, but progress in reading and writing was slow and laborious. When generalized brain damage was present significant changes did not tend to occur. 3 references. 1 table.—*Author's abstract.*

117. *Observations on the Different Diagnoses of Multiple Sclerosis and Pernicious Anemia, with Special Consideration of the Early Stages (Bemerkungen zur Differentialdiagnose zwischen multipler Sklerose und pernizioeser Anämie unter besonderer Berücksichtigung der Frühstadien).* WERNER GOTTWALD, Ansbach. Medizinische Monatschr. *7*/*8*:485–88, 1953.

It is difficult to differentiate between symptoms of multiple sclerosis and hyperchromic

pernicious anemia (Bierner) in their early stages, but the correct diagnosis is of great importance for the right therapy and hygienic measures.

The author outlines the principal criteria and syndromes of both diseases. It is known that Bierner's disease attacks especially the middle and older age groups, but it can also appear for the first time in senility. As multiple sclerosis also manifests itself in the 50 to 60 year age range, the first occurrence of suspicious symptoms should be diagnosed with great care. Both sicknesses take their course in remissions and onsets.

In the case histories of multiple sclerosis patients one finds frequent indications of allergic tendencies and focal infections as well as skin and joint affections, while patients suffering from pernicious anemia often show hormonal, and especially hyperthyroid, disturbances. The blood of patients suffering from pernicious anemia may be found practically normal in stages of complete remission; although rarely, multiple sclerosis patients may have a tendency toward hyperchromic anemia. Of diagnostic interest is the examination of the gastric juice.

Another lead to an early diagnosis is the psychic behavior. In the incipient months or years, disturbances occur in the affects, while they are rarely observed in the intellectual functions: The imminent polysclerotics appear labile, afraid, touchy, and ambivalent. A certain sexual immaturity and hysterical complexes may be premorbid constitutional characteristics. Another means of early diagnosis is the "euphoric" debility. The incipient pernicious anemia, on the other hand, creates a hypochondriac, neurasthenic, and apathic weakness, which seems to be composed of depressive and paranoid elements. This pernicious psychosis is very different from the uncritical exaltation of multiple sclerosis.

The diagnostic importance of the Hunter glossopathy and atrophy of the tongue papillae is known. Degeneration of the opticus can easily indicate pernicious anemia, but is not observed in multiple sclerosis.

The motor disturbances in the lower extremities are very similar in both pathographies, as is the condition of sensibility. Disturbances in the functions of the bladder and rectum are frequent in both sicknesses. Therefore, the fluid must be examined. It is practically always normal in funicular spinal patients. 26 references.

118. *Pyramidal Signs.* ROBERT WARTENBERG, San Francisco, Calif. Postgrad. Med. *15*: 405–409, May 1954.

To establish the presence of a pyramidal lesion in cases of hemiplegia and paraplegia the following simple tests are useful and not included in most neurologic textbooks:

1. Winking-jaw test: indicating a supranuclear lesion in the trigeminal pathways, the test is positive when on touching one cornea the mandible moves to the opposite side. This is due to a release phenomenon that associates the orbicularis oculi and external pterygoid.

2. Lid Vibration Test: even in mild or residual supra- and infranuclear lesions of the facial pathways the normal vibration of the closed upper lid is abolished. Presence or absence of vibration is felt by the examiner's thumb lightly applied to the closed lid.

3. Knee Dropping Test: with both knees slightly flexed in the recumbent position, and the heels resting on a slippery surface (e.g. talcum powder on a sheet of metal) the affected leg has a marked tendency to extend.

4. Orbicularis Oris Reflex: if you tap a tongue blade that slightly stretches the corner of the mouth you may elicit a faint twitch of the orbicularis oris muscle, i.e. mainly of the upper lip. On the hemiplegic side, however, this contraction will be quite marked, sometimes even on tapping the healthy side.

5. Pendulousness of the Legs: the patient's legs, hanging relaxed over the edge of the examining table, are passively lifted and dropped. On the side of a pyramidal lesion the resulting pendulum motion is found to occur in an irregular circle, instead of in the normal sagittal plane.

6. Head Retraction Reflex: this stretch reflex of the extensors of the head and neck is elicited as the reflex hammer strikes a light downward blow on the patient's upper lip. The patient's head is slightly bent. As the additional brisk stretching force is transmitted to the extensor muscles, they react with a brief contraction that retracts the head. Essentially a normal phenomenon, but of high threshold, the reflex is manifest only in bilateral supracervical pyramidal disease.

7. Dissociation of Abdominal Skin and Muscle Reflexes: in bipyramidal lesions above T6 the stretch reflex of the abdominal muscles, elicited by tapping, is exaggerated, while the abdominal skin reflexes, elicited by stretching, are lost.—*Author's abstract.*

119. *Spontaneous Rhythmic Ocular Movements; Their Possible Relationship to Mental Activity.* HARRY A. TEITELBAUM, Baltimore, Md. Neurology. *4*:350–354, May 1954.

Spontaneous, rhythmic ocular movements have been observed in a very high percentage of people. These movements vary in their characteristics from person to person, but have a constant pattern in any one person. The movements occur most often when people stare ahead in mental concentration and during pauses in conversation. They do occur during speech in some people. It is suggested that these movements may play the role of inhibiting visual stimuli during mental concentration, as thresholds for sensory perception are usually elevated at such times. This hypothesis may lend itself to study by means of electroencephalography. 9 references. 2 tables.—*Author's abstract.*

ANATOMY AND PHYSIOLOGY OF THE NERVOUS SYSTEM

120. *Recent Advances in Neurophysiology.* JOHN F. FULTON, New Haven, Conn. J. Neurosurg. *11*:1–6, January 1954.

Attention is drawn to the fact that a large extralemniscal ascending system, quite separate from the spinothalamic tract, can be traced through the medulla to hypothalamus, reticular formation with some fibers proceeding directly to limbic structures of the frontal lobe. A clear cut distinction can now be made between the two great systems of the forebrain: (1) the phylogenetically ancient *limbic complex*, which is concerned with autonomic reactions involved in emotional expression and only secondarily with intellectual function, and (2) the *somatic neocortex*, which presides primarily over higher intellectual functions. Both systems are to be found in the anatomic frontal lobe. Lesions restricted to the frontal limbic system cause little or no impairment in intellectual functions, such as visual discriminatory capacity, but such lesions do affect emotional behavior and to a limited extent such learned habits as those involved in double alternation.

The essential pathways to and from the limbic system pass in a discrete area in the medial ventral quadrant of the frontal lobe, which can be interrupted in both animals and man by electrocoagulation. In one of Delgado's human subjects, intractable pain was dramatically relieved by a small bilateral lesion in this area, the relief having continued for an 18 month period. The gross intellectual deterioration that follows radical lobotomy is not seen with these small medial ventral lesions.

Other advances in neurophysiology in the past five years have led to a deeper understanding of spinal reflexes and their mode of operation in the human paraplegic. There has also been notable clarification of cerebellar function and of the functional activity of the reticular formation—all of which bids fair to increase our understanding of many obscure neurologic disease entities, and through that knowledge to extend sound therapy, neurosurgical and otherwise. 26 references. 1 figure.—*Author's abstract.*

121. *Further Analysis of the Temporal Lobe Syndrome Utilizing Frontotemporal Ablations.* KARL H. PRIBRAM, MURIEL BAGSHAW, New Haven, Conn. J. Comp. Neurology. *99*: 347–375, October 1953.

Ten primates received bilateral ablations within the frontotemporal region of the cerebral hemispheres. Anatomic analysis showed lesions to be bilaterally symmetrical. Thalamic degenerations in the medial magnocellular portion of the n. medialis dorsalis, midline intralaminar, n. medialis ventralis, and medial pulvinar of the thalamus were related, respectively, to the lesions in the posterior orbital gyrus, anterior perforate substance and limen insulae, temporal polar formations, and anterolateral temporal cortex.

Performance in vision, with respect to acuity, extent of field, and ability to make discriminations, was unaffected by such lesions. No changes in ability to localize tactile stimuli were observed. Range of movement was unaltered. Performance in the delayed-reaction test was unimpaired. On the other hand, altered behavior did occur in the categories of taste, energy balance, and approach to or avoidance of a variety of stimuli, including noxious and social ones. 34 references. 7 figures. 1 table.—*Author's abstract.*

CONVULSIVE DISORDERS

122. *Incidence of Idiopathic Convulsions in Later Life.* JACK G. OATMAN, Aspinwall, Pa. Arch. Neurol. & Psychiat. *71*:181–184, February 1954.

It has been generally recognized that convulsive seizures without demonstrable organic pathology or serious systemic disease may begin in later adult life, but most writers have classified such cases as rare. Patients experiencing their first seizure in adult life should be examined with great thoroughness, but it is the author's experience that the percentage of patients having an onset of seizures later in life is distinctly higher than the figure usually quoted. Representative textbooks adhere to the traditional figure of "75 per cent before age 20."

A series of 212 patients with idiopathic convulsions were followed for periods varying from 1 to 5½ years. No patient with onset later than 45 years of age was included, nor were patients with central nervous system syphilis, brain tumors, congenital intracranial ano-

malies, proved cases of encephalitis or meningitis, patients with known history of head injury, heavy metal poisoning, or chronic alcoholism.

The diagnosis of idiopathic paroxysmal cerebral disorder was made only when the history was sufficiently typical and a complete investigation failed to disclose neurologic pathology or generalized systemic disease to account for the convulsions. No case was included if there was any reason to suspect the seizure represented a dissociative or conversion reaction. Every patient was under observation for at least three separate periods during the course of a year.

Of the 212 patients studied, the age of onset was as follows: birth to 20 years, 46 patients (21.69 per cent); 21 to 30 years, 125 patients (58.97 per cent); 31 to 40 years, 41 patients (19.34 per cent). These data reemphasize the fact that the onset of convulsions in later life is not presumptive evidence of organic brain disease and that the incidence of such phenomena in persons of more mature years without demonstrable pathology is by no means uncommon. 7 references. 2 tables.—*Author's abstract.*

DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

123. *Is Multiple Sclerosis a Manifestation of Idioblaptic Allergy?* MILO G. MEYER, ALAN JOHNSTON, ARTHUR F. COCA. Psychiatric Quart. *28*:57–71, January 1954.

This article suggests the possibility that multiple sclerosis may have an allergic etiology. The authors suggest that in its early stages the pathology of multiple sclerosis could be either on the basis of perivascular edema or marked angiospasm, such as apparently occurs in migraine.

The case presentations are thought to represent a reasonably long period of observation, with either amelioration of symptoms or a nonprogressive state while these individuals are on allergic management. It is true that intravenously administered histamine was used in the majority. The thought behind that treatment is that it not only effects vasodilatation but also, in some measure, aids in blocking the allergic response. The authors, therefore, think that further exploration into idioblapsis or nonreaginic allergy should be attempted by clinicians interested in this illness. 8 references. 1 table.—*Author's abstract.*

124. *Liver Function and Other Blood Chemistry Tests in Multiple Sclerosis.* NORMAN B. DOBIN, JOHN L. SWITZER, Chicago, Ill. Arch. Neurol. & Psychiat. *71*:405–424, April 1954.

Fifty-eight patients with multiple sclerosis were each examined for evidence of liver dysfunction by a battery of 27 chemical hepatic function tests, which were useful for other studies as well. Fourteen of this group of patients were in the acute or active phase, and 44 patients in the chronic, inactive, or slowly progressive phase of the disorder. There were 13 males and 45 female patients; their ages ranged from 18 to 64 years.

The hepatic tests were, for convenience, divided into several categories: (a) lipid studies, including phenol turbidity, total lipid turbidity, total cholesterol, free cholesterol, cholesterol esters, ratio of free cholesterol to total cholesterol, ratio of cholesterol esters to total cholesterol, and lipid phosphorus; (b) enzyme studies, including serum esterase, alkaline phosphatase, and, coincidentally, serum inorganic phosphorus; (c) bilirubin excretion in the blood

by the total van der Bergh test and in the urine by urinary bilirubin; (d) obstructive mechanisms by urinary urobilinogen; (e) detoxifying and dye excretion ability, measured by the bromsulfalein retention; and (f) plasma proteins determinations, including total protein, true albumin, true globulin, true albumin-globulin ratio, Howe albumin, Howe globulin, Howe albumin-globulin ratio, gamma globulin, mucoprotein, cephalin flocculation, thymol turbidity, and zinc sulfate turbidity.

Tests that have been reported to have a significant statistical association with liver cell damage, namely, the albumin-globulin ratio, cephalin flocculation, thymol turbidity, and bromsulfalein retention tests, and those showing a lesser degree of correlation, namely, highly elevated serum bilirubin and slightly elevated alkaline phosphatase, did not occur in statistically significant numbers in our group of 58 patients. Furthermore, the joint occurrence of abnormalities in these particular tests was also not of statistically significant magnitude.

Abnormalities of total cholesterol, cholesterol esters, lipid phosphorus, serum esterase, inorganic phosphorus, true globulin, Howe albumin, and zinc sulfate turbidity tests occurred with statistically significant frequency in the group of 58 patients studied. These abnormalities are not considered to be related to hepatic function. 43 references. 5 tables. —*Author's abstract.*

ELECTROENCEPHALOGRAPHY

125. *The Electroencephalogram in Pernicious Anemia and Subacute Combined Degeneration of the Cord.* JOHN N. WALTON, L. G. KILOH, J. W. OSSELTON, JOAN FARRALL, England. EEG Clin. Neurophysiol. 6:45–64, February 1954.

Eighty patients with pernicious anemia in relapse, of whom 24 had subacute combined degeneration of the cord (1 with optic atrophy), 41 mild neurologic involvement, and 15 none, have been studied by means of the electroencephalogram. Seven patients showed mild organic reactions, and in all of these the pretreatment record was abnormal. The pretreatment record was also abnormal in 60 per cent of the remaining patients, who showed no significant mental abnormality. In some patients abnormality was severe (delta activity, generalized, paroxysmal, or focal), in some slight (slight or moderate excess of theta activity), but the degree of abnormality bore no relationship to the severity of the anemia, the age of the patient, or the degree of neurologic involvement.

Ten patients with anemia of miscellaneous type were also studied before treatment; although in 3 of these the hemoglobin level was less than 40 per cent, only in 1 patient did the EEG show a significant abnormality, and this patient had severe hypertension and atherosclerosis.

Seventy-six of the patients with pernicious anemia were reexamined after treatment with vitamin B_{12}. In 14 of the 29 patients who gave normal records before treatment there was a significant increase in mean frequency of the alpha rhythm and diminution in over-all amplitude. Forty-two of the remaining 47 patients in whom the initial record was abnormal showed a satisfactory clinical response to treatment, and in 31 (74 per cent) the EEG returned to normal, so that 60 of the 76 patients (79 per cent) eventually gave normal records. Improvement in the record began as a rule 7 to 10 days after the beginning of treatment and

was often complete within a month, although some patients showed further improvement after intervals varying from 3 to 16 months. In the other 11 patients (26 per cent) who responded, persisting abnormalities consisted of a slight excess of generalized theta activity, a finding which in some could possibly be accounted for by age or constitution.

Another 50 patients with pernicious anemia (including 37 with subacute combined degeneration of the cord, 8 with mild neurologic involvement, and 1 with optic atrophy) were first studied after treatment had been in progress for between 3 months and 8 years (average 18 months). Excluding 5 patients showing epileptic discharges, 38 (84 per cent) of the other 45 patients had normal records; the remaining 7 patients (16 per cent) were restudied, and in all the EEG showed further improvement 5 months to 3 years after the beginning of treatment. The final total of normal records was 42 (93 per cent).

Eight (6 per cent) of the 130 patients with pernicious anemia studied gave records showing epileptic discharges (usually temporal spikes or sharp waves) and of these 4 (3 per cent) gave a personal or family history of fits or faints.

It is suggested that the EEG changes in pernicious anemia are due not to the anemia but to a specific defect in cerebral metabolism, presumably related to the deficiency state responsible for the anemia. Though not so sensitive as studies of cerebral metabolism by the blood flow method, the EEG is a useful tool in the investigation of these patients and reveals that maximum improvement may be delayed for up to 3 years after treatment has begun. The possible relationship of the EEG changes to alterations in glucose and pyruvate metabolism is discussed. 12 references. 9 figures. 10 tables.—*Author's abstract.*

126. *The Electroencephalogram in Paralysis Agitans.* DON L. WINFIELD, P. J. SPARER, Memphis, Tenn. Dis. Nerv. System. *51*:114–117, April 1954.

It has been reported elsewhere that pentothal spindles did not appear in 11 patients with Parkinsonism and chorea with sleep induced by intravenous sodium pentothal. In the present investigation sleep was induced by intravenous sodium pentothal and/or chloral hydrate. Sleep spindles were obtained in all nine sleep records. The discrepancies observed might be explained by one or more of the following:

1. Differences in the technic of inducing sleep which affect the patterns of the brain waves.
2. Difference in age.
3. Possibly greater thalamic damage in the group studied by Mallin et al.

The first is, in our opinion, the most important.

Four of our 9 patients with sleep records had the "mitten pattern" reported by Leemhuis and Stamps to be more common in Parkinsonism than in any other condition. These cases were in the arteriosclerotic group. Of 29 cases with Parkinsonism, 62 per cent showed abnormal EEG's, usually of the slightly abnormal-slow (S-1) type. 12 references. 4 figures. —*Author's abstract.*

127. *The Electroencephalogram in Manic-Depressive Psychosis.* L. A. HURST, Krugersdorp, South Africa; A. C. MUNDY-CASTLE, DIANE M. BEERSTECHER, Johannesburg, South Africa. J. Ment. Sc. *100*:220–240, January 1954.

The primary aim is to verify the claims of Pauline Davis that manic-depressive depressed

psychotics (M.D.D.'s) tend to possess lower alpha frequencies than manic-depressive manics (M.D.M.'s), and that alpha frequency does not shift with change in psychotic phase. These claims are important in relation to a report by one of the present authors (A. C. Mundy-Castle) that alpha frequency is related to the temperament variable primary-secondary function, since historically M.D.D.'s have been considered to be of secondary functioning temperament, M.D.M.'s of primary functioning. A subsidiary aim is a detailed analysis of electroencephalographic characteristics of manic-depressive psychotics, with particular reference to the applicability of the Davis "choppy" classification.

EEG's were recorded from 117 patients, with 48 repeats, using a six channel machine and for later recordings a frequency analyzer. Mean age was 55 years. The control group comprised 160 normals, mean age 22 years. Most important findings are:

(a) M.D.M.'s have a significantly higher mean alpha frequency than M.D.D.'s, and there is no shift in alpha frequency corresponding to change in psychotic phase. This confirms the Pauline Davis report.

(b) With the aid of automatic frequency analysis, and after careful examination of the records, a "low voltage fast irregular" (l.v.f.i.) classification was adopted in preference to "choppy." It was found that there are significantly more l.v.f.i. EEG's among the psychotics than the controls. This does not appear to be related to age.

(c) Incidence of abnormal (24 per cent) and questionable (21 per cent) EEG's in the psychotic group is significantly greater than among the controls; this may be partially related to difference in age.

(d) In their flicker response patterns, M.D.M.'s show a significantly greater incidence of second and third harmonics, and of following in the 14 to 26 c./sec. band, than do M.D.D.'s.

Of the above, (a) is attributed to differences in degree of the basic temperament variable secondary function, and (d) suggests underlying corresponding differences in central nervous excitability. This accords with the general hypothesis concerning secondary function.

It is suggested that a primary functioning subject who develops manic-depressive psychosis is more likely to be manic than depressed; conversely, a secondary functioning subject is more likely to be depressed than manic. Changes in phase are attributed to an extraneous factor.

The possibility that the high incidence of l.v.f.i. EEG's in the psychotic group is related to a toxic-organic pathogenesis of manic-depressive psychosis is discussed. Such a view can only be tentative. 23 references. 4 figures. 6 tables.—*Author's abstract.*

128. *Clinical Evaluation of Metrazol Activation in Electroencephalography.* WALTER J. FRIEDLANDER, San Francisco, Calif. Neurology. *4*:264–270, April 1954.

The selection of patients was based on whether it was felt that a metrazol-activated EEG would aid in arriving at a more accurate diagnosis of the presence or absence of a convulsive disorder, regardless of whether there was other neurologic disease. Out of a total of 224 patients who had metrazol-activated EEG's, a definite diagnosis of organic seizures (independent of an alcoholic history) was present in 70, while 61 had a definite diagnosis of no organic seizures or any other type of episodic disorder such as vasodepressor syncope, narcolepsy, hysterial attacks, etc. The technic of administration of metrazol was as follows:

A control EEG was obtained for a period of at least 2 minutes and then, without changing the patient's position and while continuing to run the EEG, 0.5 cc. of a 5 per cent solution of metrazol (25 mg.) was given rapidly, intravenously, every half minute until a total of 8 cc. (400 mg.) was given, or until there were definite changes in the EEG; the record was continued for at least three minutes after the infusion was ended. Sixty-three per cent of the patients with seizures had an abnormal response, i.e. spikes, paroxysmal slow activity, or spike-wave complexes; 80 per cent of the patients without seizures had no change in their EEG's during this infusion. Since the metrazol was given in equal increments of 0.5 cc. (25 mg.), a table was constructed that indicated the relation between the minimal amount of metrazol needed to produce a change in the EEG and the probability of the patient's having a convulsive disorder.

Metrazol activation is an unpleasant procedure for any patient and should be reserved for those in whom there is still a problem of diagnosis after the usual work-up, including waking electroencephalograms, has been accomplished. However, the possibility of inducing a seizure in a person without seizures using this method is so remote that this should not be a factor in deciding against doing a metrazol-activated electroencephalogram.

This series was too small to arrive at any reliable conclusions about the influence of anticonvulsant medication on metrazol activation or the usefulness of metrazol in delineating a focus of cerebral pathology. It was noted that the "seizure" group with "false negative" metrazol activated electroencephalograms had a longer average history of seizures than the "true positives" "seizure" group.

A review of the literature on metrazol-activated EEG's is included. Probably an important element in the differences in results between various series is due to a difference in the selection of cases. It is felt that the method used in this present series represents a realistic approach to the practical clinical application of metrazol activation as an aid in the differential diagnosis of convulsive disorder in adult patients. 12 references. 4 figures. 4 tables.—*Author's abstract.*

TREATMENT

129. *On the Medicinal Treatment of Myasthenia* (*Zur medikamentösen Behandlung der Myasthenia*). HELMUT BAUER, OTTO SCHMID, Hamburg, Germany. Deutsche Ztschr. f. Nervenheilk. *169*:427–437, 1953.

Experiments with pyridostigmine showed that it is possible to improve the disturbances in the muscle functions affected by myasthenia gravis pseudoparalitica more lastingly than with Prostigmin.

The treatment of this disease is still based on the finding that its weakening of the muscles can be compared clinically to curare poisoning and that therefore an efficient therapy with physostigmine is indicated. A synthetic derivative of *m*-aminophenol, i.e. Prostigmin (neostigmine), proved somewhat less toxic than physostigmine and is therefore widely used in clinical treatment. Among the newer preparations, pyridostigmine proved to have longer lasting effect than Prostigmin. In addition, it seems to be better tolerated.

In experiments with this drug on the peritoneum of rats, the author first observed that pyridostigmine took effect much later than the prompt Prostigmin reactions. The same

was found in the muscles of mastication. Pyridostigmine is only half as effective as Prostigmin; the reaction sets in later than to Prostigmin, but the duration of its effect is considerably longer than that of Prostigmin.

Clinical observations confirmed these findings. It must be stated, however, that a satisfactory effect with pyridostigmine could be obtained only in those cases where the Prostigmin test was clearly positive. No rules can be set in respect to dosages; but the good absorption of this preparation allows trial without dangerous side effects. 20 references. 9 figures.

130. *Experiences with RO-2-3059 as an Anticonvulsant.* DWIGHT M. PALMER, Columbus, Ohio. Neurology. *4*:345–349, May 1954.

A new anticonvulsant, 1-benzhydryl-3-acetylurea, known as RO-2-3059, has been used in the treatment of 43 cases of epilepsy in an out patient clinic. This report concerns a study on 20 of these patients over a period of six months.

It was found that the drug was most beneficial when 500 mg. was used in combination with 45 mg. of phenobarbital. The daily dosage varied from 500 mg. to 1,500 mg. The medication was found to be moderately effective in protecting patients against grand mal seizures, rather ineffective against temporal lobe attacks, and relatively ineffective or perhaps worthless against petit mal attacks. There was no definite evidence of side effects in the skin, gums, or bone marrow. 1 table.—*Author's abstract.*

book reviews

Man Above Humanity: A History of Psychotherapy. WALTER BROMBERG, M.D., with foreword by WINFRED OVERHOLSER, M.D. J. B. Lippincott Co., Philadelphia, 1954. Pp. 342. Price $5.75.

This volume presents a well documented and well written story of the evolution of the oldest form of treatment—psychotherapy. Doctor Bromberg, no stranger in the field of medical historical writing, traces the evolution of mental treatment from its beginnings in magic, through the "king's touch" and witchcraft, its later introduction into the ambit of medicine, its relapses into faith healing (Christian science and phrenology, for example) to its further development (Mesmer, Braid, and Charcot) into the various types of modern dynamic psychotherapy.

The historical continuity of the development is emphasized throughout; the author is constantly conscious of the fact that phenomena of thought, as of physics, have a "natural history" and that we build on the foundations erected by our predecessors.

The style is eminently readable and the facts accurate (there are 958 footnotes!), and the illustrations add considerably to the attractiveness of the volume. This book can be read with profit and pleasure by all, lay and professional, who are interested in how modern psychotherapy came to be.—*Winfred Overholser, M.D.*

The Sexual Offender and His Offenses. BENJAMIN KARPMAN, M.D. Julian Press, New York, 1954. Pp. 744. Price $10.00.

The author has for over 30 years made a special study of the psychopathology of crime, and his voluminous writings are well known to psychiatrists. In the present volume he gives us not only the results of his long studies and observations but at least thumb-nail sketches of the American literature on the subject of sexual offenses and offenders for the period 1912 to 1951.

Section 1, covering the first 289 pages, presents in condensed form such topics as definitions, types, psychiatric classification, motivations, medicolegal aspects, and prevention of sexual offenses, each chapter being followed by a succinct summary. Section 2 discusses the psychodynamics of the various sexual offenses, a "topical synopsis," a bibliography, and a subsection entitled "The Problem of the Sexual Psychopath: A Formulation." A large part of this latter portion is made up of comments by various psychiatrists on the "formulation."

Dr. Karpman is properly critical of the tendency to classify "perverted" sexual behavior as "psychopathic." He refers instead to paraphiliac neuroses, and makes out a good case for this view, a view which properly implies treatability. He is likewise critical of the legal attitude toward the offender, although it is doubtful how many would agree with his statement that "there is no more need to have laws against perversive activities than there is to have laws against any illness" (p. 486). He adds, "The proper treatment of the sexual psychopath is not confinement but psychotherapy, or better yet, proper sexual education in childhood" (p. 488). Some elaboration of this theme would be helpful, particularly an answer to the query how the "psychopath" is to be persuaded to accept psychotherapy!

About 300 brief (sometimes tantalizingly so) case histories are given.

The volume is a useful addition to the literature, particularly as it gives us the views of a long time student of the problem, despite its discursiveness in some areas and its almost telegraphic brevity in others.—*Winfred Overholser, M.D.*

Fifty Years of Medicine. LORD HORDER. Philosophical Library, New York, 1954. Pp. 70. Price $2.50.

Lord Horder is not only an eminent British physician; he is also a scholar, a master of the English language, and possessed of a philosophic bent. In these three Harben Lectures, presented at the Royal Institute of Public Health and Hygiene, he gives a pungent review of the past half century's developments in the field of medicine, developments that he not only witnessed but of many of which he was a part.

He discusses the advances in surgery and medicine, such as nutrition, physical medicine, nursing, the prolongation of life and its accompanying problems, and suggests lines of action for the future—noise abatement and eugenics, for example.

He points out some of the lessons learned from the last war, and he ends on an optimistic note: "I believe that there will emerge from these severe trials to their fortitude and to their health a group of people better fitted to arrange the pattern of their lives in the better days that we are all determined they shall have in the future."—*Winfred Overholser, M.D.*

The Psychiatric Aide: His Part in Patient Care. ALICE ROBINSON, R.N., M.S. J. P. Lippincott Co., Philadelphia, 1954. Pp. 186. Price $3.00.

In simple language, without being patronizing or coy, this book directs itself to the worker who will use it, the psychiatric aide. It is designed as a text to be used in conjunction with procedural manuals, and for this reason technical formulas are not given, but emphasis is placed on feelings—those of the patient, of the aide himself, and on the interactions that develop as a result of their communications with each other.

The stated aim of the author is the promotion of desirable attitudes toward mental illness and mental patients, and of increased personal satisfaction for individuals engaged in psychiatric care. There is a short presentation of normal growth and development, as a background for the explanation of compensatory mechanisms. The reasons for patients' behavior are explained fully enough for understanding, with realistic examples taken from the wards; but the author avoids complicated dynamics and, instead, stresses the ways in which improved behavior results from patience, kindness, and empathic management. The chapter headed "It's Not What You Do, It's How You Do It" is particularly good in its simplicity and comprehensiveness. There is considerable discussion of ethical responsibilities, covering such hazards as gossip, careless talk, tipping, etc., which are usually overlooked in the aide's manual and are so important in his everyday activities.

It is generally accepted that skills of patient care in specific therapies, as well as ward management, can best be taught in the situation where they will be used. For that reason, probably, only broad principles are referred to in these areas, and the standards emphasized are those that apply to psychiatric wards anywhere.

Integrated in the text in a manner that gives it authority is a very meaningful philosophy for the aide. The material is presented in such a way that the reader develops respect for the job he is doing. There is here no tendency to idealize, but reality is presented as a potential source of stimulation to better patient care.—*Helen S. Bahr, R.N.*

Syphilitic Optic Atrophy. WALTER L. BRUETSCH, M.D. Charles C Thomas. Springfield, Ill., 1953. Pp. 140. Price $5.50.

Syphilitic atrophy of the optic nerve is still a frequent cause of blindness. It has been estimated that in the United States alone some thirty thousand people are blind as a result of this disease. In this monograph Bruetsch reviews the pathogenesis and pathology of syphilitic optic atrophy and discusses its clinical manifestations and treatment. He recommends a total of 15 to 20 million units of penicillin as adequate treatment. Such large amounts of antibiotic may be expected to arrest the progress of the disease or in some cases actually to improve the constriction of the visual fields. Adequate treatment with penicillin may render malarial therapy unnecessary, although the author does not take a strong stand on this point.

The author's fundamental research on the nature of syphilitic optic atrophy has extended over a period of more than 20 years and has led to an entirely new concept of its pathogenesis. He has shown that the degenerative process is secondary to an inflammatory cellular reaction. Through his work the use of the term primary optic atrophy as applied to this condition has been shown to be inexact.—*George W. Weickhardt, M.D.*

Fundamentals of Neuropathology. WILLIAM BROOKS DUBLIN, M.D. Charles C Thomas, Springfield, Ill., 1954. Pp. 697 +xxiii, with 786 illustrations. Price $18.50.

The author, while presenting a thorough text on neuropathology, has at the same time attempted to break down the wall that sometimes seems to tend, at least, to set off this specialty from general pathology. He says, in the preface, "Neuropathology in its most lucid and practical form is general pathology with adequately extended consideration of the nervous system. The causes, pathogenic mechanisms, products of degeneration, and forces of repair in neuropathology are fundamentally the same as those in general pathology . . . , and the same general chemical and physical principles are at work."

The arrangement of the work is indicated by the chapter headings: Methods; Elements of the Nervous System, Normal and Pathologic; Congenital Abnormalities; Inflammations; Injuries; Tumors; Metabolic Disturbances; Disorders of Obscure Nature. An extensive bibliography (496 references) and three colored plates add much to the completeness of the volume. The entire format is quite in line with the high standards we always expect of the publisher.

The volume is a valuable contribution to the literature of a field that is steadily growing in importance.—*Winfred Overholser, M.D.*

Books Received for Review

Psychosomatics: A Medical Definition of Body-Mind Relationship. WILLIAM MALAMUD, M.D. Boston Univ. Press, Boston, 1954. Pp. 24. Price $.50.

Psicodiagnostico de Rorschach. JULIO ENDARA. Casa de la Cultura Ecuatoriana, Quito, Ecuador, 1954. Pp. 326.

Proceedings of the Third Conference on Psychosurgery. ed. by W. OVERHOLSER. Govt. Printing Office, Washington, D. C., 1954. Pp. 173. Price $1.00.

Treponematoses: A World Problem. WORLD HEALTH ORGANIZATION, Geneva, 1954. Pp. 113. Price $.50.

Expert Committee on Drugs Liable to Produce Drug Addiction. 4th report. WORLD HEALTH ORGANIZATION, Geneva, 1954. Pp. 11. Price $.25.

Problems of Consciousness: Transactions of the Fourth Conference, 1953. HAROLD A. ABRAMSON, editor. Josiah Macy Jr. Foundation, N. Y. 1954. Pp. 175. Price $3.25.

The Painful Phantom. LAWRENCE C. KOLB. Charles C Thomas, Springfield, Ill. 1954. Pp. 50. Price $1.50.

Bijdrage tot de Kennis der Techniek der Groepspsychotherapie voor Volwassenen (*Contribution to the Knowledge of Group Psychotherapy Technique*). A. C. BARENTSEN. Leiden 1953. Pp. 132.

De Vezelstructuur van de Capsula Interna en Pedunculus Cerebri bij Macaca Ira (*The Fibrous Structure of the Capsula Interna and Pedunculus Cerebri in Macaca Ira*). K. MECHELSE. Leiden 1953. Pp. 93.

De toepassing van het psychodiagnostisch onderzoek volgens Rorschach bij de geneeskundige keuring van het Marinepersoneel (*The Application of the Rorschach Psychodiagnostic Test in the Medical Examination of Naval Personnel*). C. LELY. Leiden 1953. Pp. 109.